PI and Comorbidities

Skin Infections: Potential Clues to Diagnosing PI

Crohn's Disease: A Search for Better Treatments

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PI and Comorbidities: The Diagnostic Link

**INDIVIDUALS WITH** primary immunodeficiency disorders (PIs) carry increased risk of developing a variety of comorbidities. Indeed, it is estimated approximately 20 percent of PI patients with B-cell defects (the largest number of PI patients) also suffer from inflammatory and autoimmune disorders such as skin infections and gastrointestinal issues.1 Interestingly, a PI diagnosis isn’t always a precursor to a comorbid condition. Actually, the reverse may be the case: The comorbidity could prove to be the link to an undiagnosed PI.

This is certainly the case with skin infections that, according to Bob Geng, MD, author of our article “The Link Between Primary Immunodeficiency Disorders and Skin Infections,” can lead to consideration of PIs in those undiagnosed. Dr. Geng outlines the different forms of skin infections — bacterial, fungal and viral — their causes and close association with certain types of PI. Even diagnosed PI patients and their care providers can benefit from an understanding of these all-too-common infections that can be a great cause of anxiety and concern.

Inflammatory bowel disease (IBD) affects between 19 percent and 32 percent of patients with common variable immunodeficiency.2 One IBD is Crohn’s disease, an inflammatory bowel disease that requires constant monitoring, persistent dietary and lifestyle changes and can be life-threatening. Our article “Understanding Crohn’s Disease” breaks down the subtypes of the disease that affect roughly 780,000 individuals in the U.S. While Crohn’s is not very well understood, and there is no way of preventing or curing it, there are a number of different treatments depending on the health of the patient and severity of the disease. Thankfully for those who suffer from it, scientists have put this disease at the forefront of research to find more effective treatments and even a cure.

Also in this issue, we take a look at conditions other than PI that are treated with immune globulin (IG). While corticosteroids were once considered the first line of treatment for chronic inflammatory demyelinating polyneuropathy (CIDP), our article “Improving CIDP Outcomes” explains that during the past decade or more, studies have discovered IG therapy is much more effective without the serious side effects caused by corticosteroids. Indeed, while the first intravenous IG (IVIG) product was approved by the U.S. Food and Drug Administration (FDA) to treat this rare neurological disease in 2008, patients now have more treatment options, including the most recent approval of CSL Behring’s Privigen indication. What’s more, it is expected that in the near future, FDA will approve the subcutaneous administration of IG to treat CIDP, offering these patients greater flexibility and autonomy to infuse when and where they choose.

But CIDP is far from the only indication being studied for IG therapy. In fact, thousands of clinical trials are now being conducted for various diseases. In our article “Clinical Trials of Immune Globulin,” we look at some of the more interesting trials currently underway for myasthenia gravis, neuropathy, spinocerebellar ataxia, PI, dermatomyositis, post-polio syndrome and epilepsy. And, for these and other trials that produce successful results, many patients are certain to benefit from this lifesaving therapy.

As always, I hope you gain insight from the information presented and enjoy this edition of IG Living.
SSDI vs. SSI

By Abbie Cornett

OVER THE YEARS, I have discovered many patients and their families don’t understand the difference between Social Security Disability Insurance (SSDI) and Supplemental Security Income (SSI), nor which benefits they are entitled to and when they should apply. While both federal programs are for people who are disabled, they have little else in common.

From a historical perspective, SSDI is an insurance program implemented in 1956 under Title 2 of the Social Security Act. SSI is an income supplement program implemented in 1974 under Title 16 of the Social Security Act.

SSDI pays a benefit to disabled individuals as long as they qualify by having worked long enough and paid enough Social Security tax. To be eligible, individuals must have worked at least five of the last 10 years, or 20 out of the 40 quarters before they became disabled. For individuals under 30 years old, the requirements are somewhat different since they have not been in the workforce as long. The SSDI benefit is funded by general tax revenues.

Individuals qualify for SSDI and SSI based on different income requirements. SSDI is based on work history, has no asset restrictions and allows recipients to return to minimal work. SSI payments are made to the blind, elderly and completely disabled who have a demonstrated financial need. For individuals to qualify for SSI, there are strict asset limitations (less than $2,000), and working reduces the benefit. Since SSI is a need-based program, assets must be taken into account, whereas SSDI is a benefit workers pay and qualify for through contributions paid into Social Security.

Both programs require that applicants be disabled. The law defines disability as an inability to do any substantial gainful activity by reason of any medically determinable physical or mental impairment that can be expected to result in death or that has lasted or can be expected to last for a continuous period of not less than 12 months.

Before individuals are approved for SSDI or SSI, the Social Security Administration (SSA) will evaluate their claim. During this process, SSA will look at all factors affecting individuals’ ability to work such as the severity of the condition(s), age, education, past work experience, transferable skills and whether any other substantial gainful activity can be accomplished.

Applying successfully for SSDI or SSI is dependent on establishing a paper trail. A number of preliminary steps are required to be successful in obtaining benefits:

- Speak to a doctor first. Make sure the doctor and patient are in agreement that the patient is no longer able to work.
- Gather all clinical data and test results. To obtain benefits, an individual must have a severe impairment that is supported by medically acceptable clinical and laboratory findings.
- Document all work restrictions and accommodations. It is important for the patient to demonstrate he or she is unable to continue working.

In fact, a majority of people who apply for SSDI or SSI are denied the first time. This doesn’t mean patients should give up. When an application is denied, a letter will be sent to the applicant explaining why and how to appeal the decision. An appeal must be filed within 60 days of the date the disapproval letter was received. Because many applications are denied for technical reasons, patients may want to seek legal help. Disability attorneys are familiar with the application process and can help patients with the necessary documentation.

It’s important for patients to start the application process early, and not wait until they can no longer work. Many patients postpone filing for disability as long as they can, often to their own detriment. Many times, this is because they are embarrassed about being ill or feel a sense of guilt about being unable to work. But, it is important to remember these programs were established to help the chronically ill and their families.

If you have any questions about qualifying for SSDI or SSI, please contact me.

ABBIE CORNETT is the patient advocate for IG Living magazine. She can be reached at patient advocate@igliving.com or (800) 843-7477 x1366.

These programs were established to help the chronically ill and their families.
Join the conversation! Connect with other immune globulin patients through IG Living’s Facebook page at www.facebook.com/IGLivingMagazine. See our daily posts of interesting articles and facts, as well as thought-provoking questions that you can chime in on. Following are some snapshots of what’s being discussed.

Do you qualify for Social Security Disability?

I applied the first time in 2007 and was denied, and then hired an attorney, and he filed for reconsideration and was denied again in 2009. Then, he requested a hearing in 2010 and lost again. Then, he filed an appeal and for a copy of the hearing CD, which took about 15 months for it and the permission to file. The second hearing was postponed until 2012, and we finally won. I received my first check in 2013, and this was not even for my primary immunodeficiency, which I wasn’t diagnosed with until 2014; it was for other health issues. My permanent disability was granted for three years only and then subject to review in 2016, when I was told my checks would continue. They decided not to review my case, and they might or might not review it in the future.

— Rachel D

I was denied the first time like most! Now, I’m waiting on a hearing date (14.07 — the immunodeficiency clause).

— Dave S

Invisible illness! How has it affected you?

Yes! Due to the medications I take for myasthenia gravis, my adrenal glands do not function (adrenal insufficiency). They are protectors of any kind of stress — good or bad. I have been extremely sick and have been in the intensive care unit due to this. Basically, it’s impossible to be completely stress-free. However, I am learning that I can stay away from situations that do not directly impact me and will make me ill.

— Judy S

My early years were stress-riddled. Sickness causes stress, and stress makes you sick; it can be a vicious cycle. Even with coping skills, stress is still affecting our bodies.

— Vicki DH

Have you continued working with your illness?

I worked full time as a senior graphic designer with an agency that was willing to work with me on my infusions, doctor appointments and work from home if sick. I was with them for almost 18 years, but was caught in downsizing at the end of last year. I’ve been slowly building a freelance design and fine art business since then. Working full time with common variable immune deficiency and multiple secondary illnesses is definitely not easy, but I’m thankful I have been able to manage it. Not everyone is fortunate enough to work from home or have an understanding employer for as long as I did.

— Rebecca Z

I was not able to continue working, and that was one of the hardest things I have had to do. I loved my job, and I loved what I did. Also, in this society, many people judge us on what we do or don’t do. Not looking sick also worked against me. Some even told me I was better off working so I wouldn’t spend so much time dwelling on my illness.

— Jenny G
Dr. Harville » When IVIG was introduced, its intended treatment was to replace the low IgG levels in patients with immune deficiencies. After treatment begins, patients’ IgG levels are checked periodically to ensure they are receiving an adequate dose of IVIG.

It was quickly identified that IVIG is also beneficial for some other immune-mediated conditions such as dermatomyositis. The dose for these conditions is much higher than for an immune deficiency, so it would be expected that patients would have a higher-than-normal level of IgG once therapy started. Increased levels of IgG aren’t harmful for dermatomyositis; however, there are risks associated with receiving IVIG infusions such as increased risk of developing blood clots or kidney failure. These rare adverse reactions typically would occur within 24 to 48 hours of the infusion.

Question » Is There a Problem if IgG Levels Are Above the Normal Range After Treatment with IVIG?

I have been diagnosed with Sjögren’s syndrome and dermatomyositis, and have been treated with 40 grams of intravenous immune globulin (IVIG, Privigen) every two weeks for about seven months. My IgG blood test levels are now 1,747, which exceeds the maximum amount of the normal range (600-1,714 mg/dl). Should I be concerned about this?

Leslie » No IG products contain thimerosal, so any product is fine.

Question » Is There a Preservative-Free IG Brand?

I am allergic to thimerosal, so I am looking for a preservative-free brand of immune globulin (IG), preferably subcutaneous IG.

Leslie » No IG products contain thimerosal, so any product is fine.

Dr. Riedl » It is unlikely IG is causing the proteinuria unless there is some other underlying kidney disorder. The normal kidney does not typically spill protein, and unless IgG levels are much higher than the normal range due to the infusions, there should be no reason for this to occur simply due to IG treatment. The vast majority of kidney issues associated with IG involve increases in the BUN and creatinine. I would recommend you have a kidney specialist involved with your treatment to ensure there is no other underlying medical cause for the proteinuria.

Question » What Is the Cause of Increasing Proteinuria with SCIG Therapy?

Since I have been on subcutaneous immune globulin (SCIG) therapy, I have had increasing proteinuria (protein in the urine) but no abnormality in kidney function, and no one seems concerned. I have normal creatinine and blood urea nitrogen (BUN) levels. Is the proteinuria caused by the IG protein spilling over into the urine?

Have a question? Email us at editor@IGLiving.com. Your information will remain confidential unless permission is given.

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DiGeorge Syndrome: Summary of Neurologic Issues

By Terry O. Harville, MD, PhD

IN PREVIOUS issues, we discussed features of DiGeorge syndrome (DGS) and partial DGS (PDGS) resulting from the consequences of improper timing of the sequence of events during early phases of embryonic development. We began with a discussion of the genes affected by chromosome 22q11.2 hemizygosity, and how some of these genes may be involved with the neurologic features of this complicated disease. In this column, we will summarize the major neurologic and behavioral issues associated with DGS/PDGS.

As with many medical disorders, the initial primary concerns involve the most serious features and how to provide the best treatment. With DGS/PDGS, the initial concern is the heart since before the introduction of PGF1, many infants died of cardiac malformations. Also of initial concern are immune dysfunction, which is recognized as relevant, nondetectable or mild in many, but severe and life-threatening in some; hypocalcemia due to parathyroid dysfunction; and obvious features such as cleft lip or cleft palate.

Because some DGS/PDGS infants require surgery for heart conditions, resulting in significant time spent in the ICU and sometimes prolonged periods of time on ventilators, neurologic and behavioral issues were initially considered a secondary consequence, rather than a direct consequence, of the disease and, therefore, not necessarily requiring earlier intervention. However, after DGS/PDGS patients began living longer and were monitored, it was discovered these patients expressed behavioral, neurologic and psychiatric issues that correlated with having the 22q11.2 deletion found in DGS/PDGS. Subsequently, specific genes from this region were identified (e.g., COMT and CRKL), which are implicated in neurologic and psychiatric diseases.

Unfortunately, essentially all patients with DGS/PDGS will be at risk for some form of neurologic or behavioral problems, and these can include psychiatric issues. Therefore, children with DGS/PDGS must be evaluated early and enrolled in special education programs to offset these deficits.

While relatively rarer in children, it is thought that 60 percent of patients with DGS/PDGS will eventually be diagnosed with a psychiatric illness by adulthood. Those with lower IQ levels are at higher risk. As such, children with DGS/PDGS should be evaluated by psychiatric specialists to assess their risks, and followed over time so that a transition into psychiatric disease is not missed and specific treatment can begin earlier in the course of disease.

Unfortunately, essentially all patients with DGS/PDGS will be at risk for some form of neurologic or behavioral problems, and these can include psychiatric issues.

Today, it is known that neurologic problems and subsequent psychiatric disease are major complications in patients with DGS/PDGS, and more needs to be done earlier to mitigate these issues.

In the next issue, we will discuss more of the problems and issues that occur due to improper timing of the sequence of events during early phases of embryonic development.

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Clinical Trials of Immune Globulin

By Michelle Greer, RN, and Elissa Ritt, DHSc

PLASMA THERAPIES such as immune globulin (IG) treat rare diseases, which are defined as those that affect fewer than 200,000 people in the U.S. Because so few individuals are diagnosed with rare diseases, finding patients to enroll in clinical trials for these conditions can be challenging. Nevertheless, there are currently thousands of trials being conducted to test the safety and effectiveness of IG therapy for many disease states that can be found at ClinicalTrials.gov, a database of clinical trials around the world that are in various phases and are either soon to be recruiting, enrolling, active, completed, suspended or terminated. This site can be searched by condition, medication, location and a host of other key terms. Here, we take a look at some of the more interesting IG therapy trials currently underway.

Myasthenia Gravis (MG)
MG, a long-term neuromuscular disease that leads to varying degrees of skeletal muscle weakness, is commonly treated with intravenous IG (IVIG), even though MG is not an approved indication for the drug by the U.S. Food and Drug Administration. Because off-label usage can be problematic to obtain insurance coverage, IG manufacturers are trying to remedy this situation by conducting trials of IG therapies to treat MG.

Grifols is conducting its Efficacy and Safety of IGIV-C in Corticosteroid Dependent Patients with Generalized Myasthenia Gravis to assess whether IVIG is safe and effective in reducing steroid use in MG patients. The Phase II study that began in June 2015 is currently recruiting patients and is projected to end in July 2018.

Grifols is also sponsoring a more traditional safety and efficacy study of MG titled A Study to Evaluate the Efficacy and Safety of IGIV-C in Symptomatic Subjects with Generalized Myasthenia Gravis. This Phase II study began in July 2015 and is projected to end in January 2018.

In May, CSL Behring completed a Phase II study that began in January 2015 titled Open Label Study of Subcutaneous Immunoglobulin (SCIG) in Myasthenia Gravis. The study enrolled 25 participants who received weekly infusions of the company’s SCIG product Hizentra. No results have yet been posted.

Neuropathy
CSL Behring has partnered with the University of South Florida to conduct a Phase III study of IG to treat chronic inflammatory demyelinating polyneuropathy (CIDP), an autoimmune neurological disorder that causes limb weakness and numbness. Titled A Study of Subcutaneous Immunoglobulin as Chronic Treatment for Patients with Chronic Inflammatory Demyelinating Polyneuropathy, it is investigating the efficacy, safety and patient satisfaction measures to determine if SCIG (Hizentra) is a safe and efficacious alternative to IVIG in treating CIDP. Recently, CSL Behring received FDA approval for its IVIG product Privigen to treat CIDP based on two successful Phase III trials titled Polynueropathy and Treatment with Hizentra (PATH) and Privigen Impact on Mobility and Autonomy. The PATH study used Privigen as a placebo to Hizentra (see CSL Behring’s Privigen Now Approved to Treat CIDP on page 12).

Two European studies sponsored by European academic institutions, while not available for enrollment in the U.S., could have implications in the treatment of patients with chronic neuropathies. The first is a French study titled Biomarker Study: Predict Intravenous Immunoglobulin Responders in Chronic Inflammatory Demyelinating Polyradiculoneuropathy. While IVIG is known to be effective in the treatment of CIDP, it does not work for every patient. Therefore, the objective of this Phase II study is to identify biomarkers within IVIG-treated CIDP patients that may predict whether a patient will respond to treatment.

The second is a Phase II trial being conducted at an academic institution based in the Netherlands to determine how small fiber neuropathy (SFN) patients respond to IVIG. Investigators of the Intravenous Immunoglobulin Therapy for Small Fiber Neuropathy (IVIG-SFN) will evaluate whether IVIG alleviates SFN pain more than a placebo. SFN is the most common cause of neuropathic pain, and it is theorized the characteristic nerve damage is immunological in some patients. In these specific patients who have idiopathic SFN, IVIG could play an important role in pain reduction.

Spinocerebellar Ataxias (SCA)
Shire is co-sponsoring a Phase I trial with the University of South Florida titled An Open-Label Trial of Immune Globulin (IVIG) in Treating Spinocerebellar Ataxias. SCAs are a group of diseases characterized by brain degeneration and associated symptoms such as coordination and balance problems, poor hand-eye coordination and abnormal speech. The objective of this study is to determine how IVIG (Gammagard Liquid 10%) affects SCA symptoms and
nervous system function in patients with certain types of SCA. The currently recruiting trial began in April 2015, and is continuing despite its estimated completion date of December 2016.

Primary Immunodeficiency (PI)

CSL Behring is conducting a study titled Safety and Tolerability of Higher Infusion Parameters of IgPro20 (Hizentra) in Subjects with Primary Immunodeficiency to assess the safety and efficacy of higher Hizentra infusion rates in patients with PI. The company intends to enroll 45 patients in the currently recruiting Phase IV trial that consists of three arms with different weekly volumes and flow rates per subcutaneous injection. The study, which began in January 2017, is open to individuals 2 years and older.

Dermatomyositis

Octapharma is conducting a study to assess the safety and efficacy of Octagam 10% in patients with dermatomyositis, one of a group of muscle diseases known as inflammatory myopathies that are characterized by chronic muscle inflammation. The Phase III Study Evaluating Efficacy and Safety of Octagam 10% in Patients with Dermatomyositis (Idiopathic Inflammatory Myopathy [IIM]), which began in February 2017 and is projected to end in March 2019, could result in an important advancement in the treatment of dermatomyositis.

Post-Polio Syndrome (PPS)

One of the more unusual uses for IG therapy is in patients with PPS, a condition mainly characterized by new weakening in muscles that were previously affected by the polio infection and in muscles that seemingly were unaffected. PPS is a rare condition sometimes treated off-label with IG. Grifols is sponsoring the trial titled Study of the Efficacy and Safety of Immune Globulin Intravenous (Human) Flebogamma 5% DIF in Patients with Post-Polio Syndrome (PPS), also known as the FORCE study, to assess the optimal dose of a 5% IVIG product to achieve an improvement in functionality in PPS patients. This currently recruiting Phase II and III study, which began in July 2014 and is estimated to end in September 2020, has two arms using different dosing strategies.

Epilepsy

Epilepsy can have a multitude of causes, and it is believed immune-mediated epilepsy may respond to IG therapy. The Mayo Clinic and Grifols are conducting a study titled IVIG in Patients with VGKC Ab Associated Autoimmune Epilepsy to assess whether IVIG reduces the number of seizures in these patients. This Phase III study began in February 2016 and is expected to end in August 2018.

Phases of Clinical Trials

Clinical trials are conducted in phases, with each serving a different purpose to help researchers answer different questions. While most clinical trials recruit larger groups of people as phases progress, trials of rare diseases often involve a much smaller pool of participants.

**Phase I**: Examines initial effects and safety; evaluates the safety of increasing doses; assesses how the drug interacts with the body (pharmacokinetics and pharmacodynamics); may provide preliminary evidence of effectiveness

**Phase II**: Usually enrolls patients in larger numbers than Phase I; evaluates initial efficacy; continues safety assessments from Phase I; Phase IIA studies dosing requirements; Phase IIB studies efficacy; some trials combine Phases I and II

**Phase III**: Randomized, controlled multicenter trials in larger numbers; confirms the effectiveness of the product and general safety versus a placebo or another treatment; two or more successful Phase III trials are typically required for regulatory approval of a treatment

**Phase IV**: Trials for a drug after approval by the U.S. Food and Drug Administration and made available to the public; collects additional evidence on risks and benefits


Keeping Abreast of Current Trials

Clinical trials can help to accelerate progress and provide valuable insight into potential treatments. These are just a smattering of some of the more interesting clinical trials being conducted to test the safety and efficacy of IG therapy for a host of rare diseases. Individuals interested in clinical trials that pertain to their diagnosis can visit ClinicalTrials.gov and search criteria relevant to their situation. With the thousands of studies currently being conducted with this lifesaving medication, the future seems certain to offer treatment needed by so many patients.

MICHELLE GREER, RN, is senior vice president of sales for NuFACTOR Specialty Pharmacy.

ELISSA RITT, DHSc, is the medical science liaison for NuFACTOR Specialty Pharmacy.
Medicines

**CSL Behring’s Privigen Approved to Treat CIDP**

The U.S. Food and Drug Administration (FDA) has approved Privigen (immune globulin intravenous [human] 10% liquid) to treat adults with chronic inflammatory demyelinating polyneuropathy (CIDP) to improve neuromuscular disability. Approval is based on two Phase III studies: Polyneuropathy and Treatment with Hizentra (PATH) and Privigen Impact on Mobility and Autonomy (PRIMA). In the PATH study, 73 percent of 207 CIDP patients receiving Privigen (given as a placebo to Hizentra) responded to treatment as measured by their adjusted score on the Inflammatory Neuropathy Cause and Treatment scale. In the PRIMA study, 61 percent of 28 patients responded to treatment.

“It is a priority in the care of CIDP patients to provide therapies that improve and maintain their strength and function while at the same time preventing relapses and minimizing side effects. However, current treatments do not work for all CIDP patients,” said Mazen M. Dimachkie, professor and director of the neuromuscular division, executive vice chairman in the department of neurology at the University of Kansas Medical Center, and an investigator in the PATH study. “Privigen’s approval by the FDA for the treatment of CIDP means that people with CIDP and their treating physicians have gained another treatment option that is safe and effective in helping improve strength and motor function, while potentially delaying disease relapse.”


Research

**Study Finds PI Patients at Increased Risk of Cancer**

A new study shows that patients with primary immunodeficiency disease (PI) are at increased risk of certain cancers, most notably lymphoma. In the study, researchers compared rates of cancer in 3,658 PI patients with an age-adjusted general population from the National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) database. They found a 1.42-fold excess relative risk of cancer in subjects with PI compared with the age-adjusted SEER population. Specifically, men with PI had a 1.91-fold excess relative risk of cancer, and women showed similar cancer rates. But there was a 10-fold increase in lymphoma in men with PI and an 8.34-fold increase in lymphoma in women with PI, largely in those diagnosed with common variable immunodeficiency (CVID).

Overall, there was a 42 percent increase in cancer incidence among PI patients. The majority of cancers were comprised 70 percent of those in the database, including an increased risk of non-Hodgkin lymphoma, gastric cancer and skin cancer. Other types of PI included hypogammaglobulinemia, agammaglobulinemia and Wiskott-Aldrich syndrome. The cancer types with the highest incidence rates among PI patients in the USIDNET registry were lymphoma, skin cancer and thyroid cancer.

The researchers say two major factors appear to drive increased cancer risk: defective DNA repair and failure to provide immune surveillance against chronic viral infections such as Epstein-Barr virus and human papillomavirus, which cause cancer.

Resource

**IDF’s Redesigned Website Provides Streamlined Tools for PI Patients**

The Immune Deficiency Foundation (IDF) has redesigned its website (primaryimmune.org) to make it easier for primary immunodeficiency (PI) patients to access its programs, resources and services. The site uses a mobile-first design to streamline menus and make navigation accessible from all mobile devices. Redesigned sections include:

- **My Account**, which allows individuals to register for events, order publications, submit questions and update mailing preferences;
- **About Primary Immunodeficiencies**, which provides an overview of PI, general information on the immune system and in-depth information about specific disease types;
- **Living with PI**, which provides age-specific information ranging from sending a child with PI to school to dealing with PI in the workplace;
- **Education and Events**, where individuals can download or order IDF publications, watch educational videos and register for IDF events;
- **Stay Informed**, which provides the latest news in the PI community; and
- **Get Involved**, where PI patients can sign up to be an IDF volunteer and receive IDF Action Alerts and share their stories to inspire others.

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**Legislation**

**Illinois Passes Law Requiring Insurers to Cover Treatment for PANS/PANDAS**

In July, Illinois became the first state to enact a law requiring insurers to cover medical treatment for pediatric acute-onset neuropsychiatric syndrome (PANS) and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infection (PANDAS). Known as “Charlie’s Law,” Governor Bruce Rauner signed the bill into law in Lombard at the kitchen table of Charlie Drury, a 12-year-old who suffered a debilitating mental illness after a case of strep throat. The autoimmune disorders affect one in every 200 children in the U.S., with each treatment costing up to $15,000.

The new law applies to all group and individual policies of accident and health insurance or managed care plans that are amended, delivered, issued or renewed after July 18, 2017, in Illinois; insurers for Illinois state, county and municipal employees; and insurers provided through the Illinois School Code, the Limited Health Service Organization Act and the Voluntary Health Services Plans Act. It does not apply to self-insured, nonpublic employers; self-insured health and welfare plans such as union plans; and insurance policies or trusts issued in other states.

Coverage for treatment of PANDAS/PANS includes, but is not limited to, the use of intravenous immune globulin (IVIG). While insurers can still deny claims subject to the exclusions in a policy, they can’t deny IVIG treatment as medically unnecessary or as experimental and/or investigational since the statute specifically provides for IVIG. Co-shopping practices such as copays, deductibles and/or coinsurance still apply under the terms of the insurance policy.

According to Wendy Nawara of the PANDAS/PANS Advocacy and Support group, the law “will help numerous other families in the state. Not only will it affect the families, but it will encourage the doctors to learn more about PANDAS/PANS so that they can treat it more expeditiously and get these kids what they need.” Nawara says she expects other states to follow suit.

**Registry**

**AARDA Launches Registry for MS Patients**

The American Autoimmune Related Disease Association (AARDA) has launched the first registry for patients with multiple sclerosis (MS) and other autoimmune diseases (ADs) in honor of National Autoimmune Disease Awareness Month in March. The Autoimmune Research Network (ARNet) aims to boost research by creating a comprehensive, central database of anonymous patient information. ARNet’s goal is to help researchers answer epidemiological questions, identify trends and track how patients with autoimmune diseases are experiencing the path to a correct diagnosis. The database will also allow researchers to query data sources to find individuals who might qualify for a clinical trial based on their profiles. “With this ‘big data’ project, AARDA’s hope is to drive much-needed clinical research into the numerous and wide-ranging ADs,” said Virginia T. Ladd, AARDA’s founder and executive director. “This research ultimately will help improve time to diagnosis of these diseases, as well as advance knowledge into causes, treatments and, perhaps, cures.”

Individuals can register online at the AARDA’s website (www.aarda.org) or at websites of participating National Coalition of Autoimmune Patient Groups websites.

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**IN THE NEWS**
Experts Revised PANS/PANDAS Treatment Guidelines

Experts in the PANS Research Consortium have revised treatment recommendations for children with pediatric acute-onset neuropsychiatric syndrome (PANS) and pediatric autoimmune neuropsychiatric syndrome associated with streptococcal infection (PANDAS). The recommendations, published on the *Journal of Child and Adolescent Psychopharmacology* website, break down treatment into three parts: part one — psychiatric and behavioral interventions; part two — immuno-modulatory therapies; and part three — treatment and prevention of infections. In part one, symptom improvement is aimed at decreasing suffering, improving function and making it easier for children to adhere to therapeutic interventions. Part two provides recommendations to help guide the use of therapies targeting the neuroinflammation and post-infectious autoimmunity that are common in PANS/PANDAS. And, part three presents a consensus guideline for managing the infection components of the conditions. The full article on treatment guidelines can be accessed at online.liebertpub.com/doi/full/10.1089/cap.2017.0042.

The Skin IS the body’s first line of immunity against infectious agents. During a breach of this immune system, infections of the skin affect a person’s appearance, often leading to great anxiety and concern. Unfortunately, these invasive infections are all too common among individuals with primary immunodeficiency disorders (PIs). Patients with certain types of PI are known to be more prone to certain types of bacterial, fungal and viral skin infections. For this reason, recognition of various skin infections can help provide clues to potential defects in the immune system, which can lead to consideration of PIs in those undiagnosed.

**Bacterial Infections**

Bacterial skin infections vary based on extent and depth of infection. They can range from mild folliculitis (inflammation/infection of skin follicles) to deep cutaneous abscesses. The most common types of bacteria that invade the skin include Staphylococcus and Streptococcus species. Critical first responders in the immune system that help to defend against bacteria that invade the skin are the phagocytes, including neutrophils and macrophages. No doubt, defects of the function of phagocytes often lead to bacterial skin infections.

**Understanding what types of immune system defects may be the cause of skin infections can help in the diagnosis of a primary immunodeficiency disorder.**
One of the most well-known PI conditions related to phagocytic dysfunction is chronic granulomatous disease (CGD). CGD is characterized by a defect in the phagocyte’s ability to generate reactive oxygen species to kill microorganisms that have been ingested by the phagocyte. CGD affects many organ systems and has both infectious and noninfectious (autoimmune) complications. However, skin infections are often the most noticeable and are frequently the complications that prompt patients to seek medical attention. The most common bacterial complications in CGD range from cellulitis (noncontagious spreading infection) and impetigo (contagious skin infection) to abscesses (tender, soft swellings filled with pus, often surrounded by an area of skin colored from pink to deep red). And, the most frequent culprit bacterial skin infection organism is generally Staphylococcus aureus.

In order for phagocytes to eliminate bacteria properly, they have to produce the reactive oxygen species, get to the location of the bacteria and then traffic the reactive oxygen species to the engulfed bacteria. Defects in either one of those processes can lead to susceptibility to bacterial infections. Chediak-Higashi syndrome (CHS) is a condition caused by a defect in lysosome fusion, which leads to the inability to move the reactive oxygen species in lysosomes to the engulfed bacteria. Patients with CHS develop pyogenic (pus-forming) skin infections that range from superficial to deep skin abscesses. The inciting organisms are often Staphylococcus or Streptococcus. Leukocyte adhesion disorder (LAD) is a condition in which the phagocytes cannot move out of the blood vessel to get to the site of infection. There are three subtypes of LAD, but they are generally all associated with bacterial skin infections without pus formation since the phagocytes cannot get to the actual location of the infections. Both CHS and LAD are extraordinarily rare disorders with many more severe clinical manifestations that extend beyond skin infections.

One of the key signals that activate the neutrophils and overall immunity in the mucosal and skin surfaces is interleukin-17 (IL-17). Defects in the activity or production of IL-17 will lead to susceptibility to bacterial skin infections, as well as fungal infections. The autosomal dominant hyper-IgE syndrome, otherwise known as Job’s syndrome, is caused by a defect in one of the cell signaling proteins STAT3, which ultimately leads to a deficiency in production of IL-17. Job’s syndrome, as the name suggests, is associated with skin abscesses, furuncles, cellulitis and lymph node infections caused by Staphylococcus organisms.

In addition to the specific disorders that have hallmark features of bacterial skin infections, PI’s that lead to significant humoral/antibody deficiency, T-cell deficiency and combined humoral and cellular immunodeficiency may also impair the body’s ability to fight off bacteria that invade the skin and increase susceptibility to skin infections.

**Fungal Infections**

As previously discussed, IL-17 plays an integral role in mucosal and cutaneous (skin) immunity. Because Job’s syndrome can increase susceptibility to bacterial skin infections, the risk of candidal (yeast) infections on the skin is also increased. Other PI syndromes that are associated with IL-17 defects include the AIRE (autoimmune regulator) mutation and the IL-17 receptor mutations. These conditions lead to a condition called chronic mucocutaneous candidiasis (CMC), which is a chronic fungal infection of the skin, nails and mucosa (oral and urogenital). CMC, in general, is limited to the skin and mucosa, and most cases do not tend to lead to systemic fungal infections, although in a minority of cases systemic infection has been reported. The AIRE mutation leads to neutralizing autoantibodies that inhibit the function of IL-17. The IL-17 receptor mutations lead to impaired binding of IL-17 to its target, diminishing its function. Another relatively recently discovered defect of the IL-17 pathway is the STAT-1 gain-of-function (GOF) mutation. While STAT-1 GOF can lead to an overactivation of the intracellular signaling protein STAT-1, the end result is an impairment in the production of IL-17 pathway signaling molecules.

**The most common types of bacteria that invade the skin include Staphylococcus and Streptococcus species.**

The body recognizes general patterns of fungal organisms using pattern recognition receptors. These receptors, which can bind to common components of fungal cell wall, work together with another receptor called dectin-1 to enhance the recognition of fungal organisms, leading to adequate immunity against these infections. Therefore, mutations that affect the function of dectin-1 leading to deficiency would reduce antifungal immunity. Interestingly, dectin-1 deficiency has only been described to be associated with CMC, and not invasive systemic fungal infections.
Important Safety Information

Hizentra treats various forms of primary immunodeficiency (PI) in patients age 2 and over.

WARNING: Thrombosis (blood clotting) can occur with immune globulin products, including Hizentra. Risk factors can include: advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (blood thickness), use of estrogens, installed vascular catheters, and cardiovascular risk factors.

If you are at high risk of thrombosis, your doctor will prescribe Hizentra at the minimum dose and infusion rate practicable and will monitor you for signs of thrombosis and hyperviscosity. Always drink sufficient fluids before administration.

Tell your doctor if you have had a serious reaction to other immune globulin medicines or have been told you also have a deficiency of the immunoglobulin called IgA, as you might not be able to take Hizentra.

You should not take Hizentra if you know you have hyperprolinemia (too much proline in your blood).

Infuse Hizentra under your skin only; do not inject into a blood vessel.

Allergic reactions can occur with Hizentra. If your doctor suspects you are having a bad allergic reaction or are going into shock, treatment will be discontinued. Immediately tell your doctor or go to the emergency room if you have signs of such a reaction, including hives, trouble breathing, wheezing, dizziness, or fainting.

Tell your doctor about any side effects that concern you. Immediately report symptoms that could indicate a blood clot, including pain and/or swelling of an arm or leg, with warmth over affected area; discoloration in arm or leg; unexplained shortness of breath; chest pain or discomfort that worsens with deep breathing; unexplained rapid pulse; and numbness or weakness on one side of the body. Your doctor will also monitor
Before being treated with Hizentra, inform your doctor if you are pregnant, nursing or plan to become pregnant. Vaccines (such as measles, mumps and rubella) might not work well if you are using Hizentra. Before receiving any vaccine, tell the healthcare professional you are being treated with Hizentra.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

symptoms that could indicate hemolysis (destruction of red blood cells), and other potentially serious reactions that have been seen with Ig treatment, including aseptic meningitis syndrome (brain swelling); kidney problems; and transfusion-related acute lung injury.

The most common drug-related adverse reactions in the clinical trial for Hizentra were swelling, pain, redness, heat or itching at the site of injection; headache; back pain; diarrhea; tiredness; cough; rash; itching; nausea and vomiting.

Hizentra is made from components of human blood. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

Before being treated with Hizentra, inform your doctor if you are pregnant, nursing or plan to become pregnant. Vaccines (such as measles, mumps and rubella) might not work well if you are using Hizentra. Before receiving any vaccine, tell the healthcare professional you are being treated with Hizentra.

Please see brief summary of full prescribing information for Hizentra on adjacent page. For full prescribing information, including boxed warning and patient product information, please visit Hizentra.com.

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*Voice2Voice advocates are not healthcare professionals or medical experts. For medical questions, please contact your physician. Voice2Voice advocates are compensated by CSL Behring LLC for their time and/or expenses.

Hizentra®, Immune Globulin Subcutaneous (Human), 20% Liquid
Initial U.S. Approval: 2010

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use HIZENTRA safely and effectively. See full prescribing information for HIZENTRA.

WARNING: THROMBOSIS
See full prescribing information for complete boxed warning.

- Thrombosis may occur with immune globulin products, including Hizentra. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors.
- For patients at risk of thrombosis, administer Hizentra at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

INDICATIONS AND USAGE

Hizentra is an Immune Globulin Subcutaneous (Human) (IGSC), 20% Liquid indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.

Dosage and Administration

For subcutaneous infusion only.

Administer at regular intervals from daily up to every two weeks (biweekly).

DOSAGE (2.2)

Before switching to Hizentra, obtain the patient’s serum IgG trough level to guide subsequent dose adjustments.

- Weekly: Start Hizentra 1 week after last IGIV infusion
  Initial weekly dose = Previous IGIV dose (in grams) x 1.37
  No. of weeks between IGIV doses
- Biweekly: Start Hizentra 1 or 2 weeks after the last IGIV infusion or 1 week after the last weekly Hizentra/IGIV infusion. Administer twice the calculated weekly dose.
- Frequent dosing (2 to 7 times per week): Start Hizentra 1 week after the last IGIV or Hizentra/IGSC infusion. Divide the calculated weekly dose by the desired number of times per week.
- Adjust the dose based on clinical response and serum IgG trough levels.

Administration

- Infusion sites – 1 to 4 injection sites simultaneously, with at least 2 inches between sites.

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<tr>
<th>Infusion Parameters*</th>
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As tolerated

INDICATIONS AND USAGE

Hizentra® is indicated for the treatment of primary immunodeficiency (PI) in adults and pediatric patients 2 years of age and older.

The passive transfer of antibodies may interfere with the response to live virus vaccines, and drugs may interfere with the response to antiviral vaccines.

DOSE AND ADMINISTRATION

For subcutaneous infusion only.

Administer at regular intervals from daily up to every two weeks (biweekly).

DOSAGE (2.2)

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- Weekly: Start Hizentra 1 week after last IGIV infusion
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- Adjust the dose based on clinical response and serum IgG trough levels.

Dosage Forms and Strengths

0.2 g per mL (20%) protein solution for subcutaneous injection

CONTRAINDICATIONS

- Anaphylactic or severe systemic reaction to human immune globulin or components of Hizentra, such as polysorbate 80
- Hyperprolinemia (type I or II) (Hizentra contains the stabilizer L-proline)
- IgA-deficient patients with antibodies against IgA and a history of hypersensitivity

WARNINGS AND PRECAUTIONS

- IgA-deficient patients with anti-IgA antibodies are at greater risk of severe hypersensitivity and anaphylactic reactions.
- Thrombosis may occur following treatment with immune globulin products, including Hizentra.
- Aseptic meningitis syndrome has been reported with IGIV or IGSC treatment.
- Monitor renal function, including blood urea nitrogen, serum creatinine, and urine output in patients at risk of acute renal failure.
- Monitor for clinical signs and symptoms of hemolysis.
- Monitor for pulmonary adverse reactions (transfusion-related acute lung injury [TRALI])
- Hizentra is made from human plasma and may contain infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

ADVERSE REACTIONS

The most common adverse reactions observed in ≥5% of study subjects were local reactions (i.e., swelling, redness, heat, pain, and itching at the injection site), headache, diarrhea, fatigue, back pain, nausea, pain in extremity, cough, rash, pruritus, vomiting, abdominal pain (upper), migraine, and pain.

To report SUSPECTED ADVERSE REACTIONS, contact CSL Behring Pharmacovigilance at 1-866-915-6958 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Pediatric: No specific dose requirements are necessary to achieve the desired serum IgG levels.

Based on October 2016 revision
Cellular immunity is crucial in antifungal immunity. Deficiencies in cellular immunity lead to an increased susceptibility to fungal infections. Classical severe combined immunodeficiency (SCID) and hypomorphic (leaky) SCID patients will have a greater predisposition to developing fungal skin infections. Other forms of combined cellular/humoral immunodeficiency disorders and predominately cellular immunodeficiency disorders can also lead to CMC. A few examples of these conditions include Wiskott-Aldrich syndrome, dedicator-of-cytokinesis 8 deficiency (DOCK8), DiGeorge syndrome, etc.

**Viral Infections**

Viral infections of the skin can be broadly categorized into those caused by herpes viruses, poxviruses and papillomaviruses. Key parts of the immune system that help control viral infections are T cells (both T-helper as well as T-cytotoxic) and natural killer (NK) cells. PIs that decrease the number of these cells or disrupt/impair their function will increase susceptibility to developing viral skin infections.

The most common herpes viruses are herpes simplex virus (HSV) 1 and 2 and herpes zoster. Following primary infection, herpes viruses generally reside in a dormant state in the cell bodies of neurons. Both herpes simplex and zoster can reactivate depending on degree of stress or immunodeficiency. While there are systemic symptoms associated with primary infection, reactivation is generally limited to skin symptoms such as the development of a burning, painful red rash with vesicles (fluid- or air-filled sacs). Generally, reactivation of herpes simplex is in the same area or a nearby area to the primary infection. Herpes zoster reactivation generally is isolated to a particular dermatome nerve distribution (an area of the skin that is supplied by a single spinal nerve) on one side of the body. Herpes zoster reactivation can occur in immunocompetent individuals under periods of high stress, but immunodeficiency will increase the risk and rate of reactivation. Defects in cellular immunity will lead to more frequent and greater severity and possibility of systemic complications of both HSV and zoster.

The most common poxvirus-induced skin disease is molluscum contagiosum, which is characterized by flesh-colored dome-shaped papules with a central dimple. Molluscum is a common skin infection in childhood, but can also be seen in adults. It is spread by skin-to-skin contact, so sexual contact and contact sports are often risk factors in immunocompetent patients. Immunodeficiency can increase the risk of developing molluscum, particularly conditions that are associated with defects in T-cell function. Examples of PIs that are associated with increased risk of molluscum are Wiskott-Aldrich syndrome and DOCK8 deficiency.

The most common skin condition caused by herpes papillomaviruses (HPVs) are warts. T cells and NK cells help to control HPV infections, and PIs that lead to defects in their function will often predispose individuals to develop more significant and extensive HPV infections. Primary NK cell deficiency and DOCK8 deficiency have been associated with refractory and, often, extensive warts all over the body. One syndrome called warts, hypogammaglobulinemia, infections and myelokathexis (WHIM) is particularly associated with increased susceptibility to HPV infections. In WHIM, the defect is in a chemokine (signaling protein) called CXCR4. This syndrome affects cellular and humoral immunity (antibody production) and can lead to retention of mature neutrophils in the bone marrow, leading to low levels of neutrophils in the peripheral blood.

Another distinct condition associated with increased uncontrolled HPV infection is epidermodysplasia verruciformis (EV). EV can have a variety of presentations, including flat skin lesions to reddish-brownish plaques to warts. The primary defect in EV does not appear to be a cellular immunodeficiency, but rather a defect in restricting HPV’s access to zinc. The defect in EV is related to mutations in either the EVER1 or EVER2 gene. The normal function of these genes leads to encoding of proteins that would restrict the ability of HPV to access cellular zinc stores, which are necessary for function of various viral proteins. EV patients are at an increased risk to develop squamous cell cancers of the skin.

**The Diagnostic Link**

The skin is the most visible organ in the body and also serves as the first line of defense in our immune system. There are many key skin infections seen in a variety of PI disorders. By considering the mechanism in which a normal functioning immune system defends against various microorganisms, it’s possible that specific skin infections may offer diagnostic clues to the type of PI a patient may have. Therefore, prompt recognition of severe, unusual or recurrent skin infection/disease will alert us to the possibility of systemic illness and underlying immunodeficiency disorders.

**BOB GENG, MD, MA,** studied medicine at Washington University School of Medicine in St. Louis, where he also completed his residency training in internal medicine. He is currently an assistant professor in allergy and immunology at the University of California, San Diego. Dr. Geng received his bachelor's and Master of Arts degrees in Georgetown University’s School of Foreign Service.
A considerable amount of research is being conducted to determine the causes, as well as more effective treatments, for this sometimes life-threatening chronic illness.

By Jim Trageser
WITHOUT A CLEAR understanding of its underlying causes, a cure or even a single test to make a diagnosis, Crohn’s disease remains a baffling chronic illness that presents many primary immunodeficiency patients and their physicians with an ongoing set of challenges for addressing its significant health risks. This inflammatory bowel disease (IBD) initially manifests as gastrointestinal (GI) distress, but it can progress to life-threatening blockages and ulcers, requiring emergency surgical intervention. Even in the majority of cases, when patients enjoy long periods of remission, Crohn’s requires constant monitoring and persistent dietary and lifestyle changes that demand close cooperation between patients and their physicians.

What Is Crohn’s Disease?

Crohn’s was first described as a specific subset of IBD in a 1932 article written by Burrill Bernard Crohn, MD, of New York City’s Mount Sinai Hospital. A follow-up paper was cowritten with fellow physicians Leon Ginzburg and Gordon Oppenheimer, but Crohn’s name was listed first due to alphabetical precedent, and the condition became known as Crohn’s disease.

Crohn’s is a chronic IBD that affects the lining of the digestive tract. Any part of the GI system can be affected, from the mouth to the anus, although the most common areas affected are the lower large intestine near the anus (the sigmoid colon), and the area of the small intestine nearest the large intestine (the ileum). Crohn’s is differentiated from other IBDs by the specific type of lesions found in the digestive tract, as well as the types of ulcers and fistulas that develop in severe cases.

Mild cases affect only the innermost layer of the GI tract, the mucosa, which becomes inflamed. However, the disease can also affect deeper layers, and in severe cases becomes life-threatening due to the development of blockages, ulcers or fistulas that can require surgery to repair. Healthy segments of the intestines can exist alongside diseased segments, with abrupt transitions between affected and healthy tissue. Children with the disease often exhibit stunted growth and delayed puberty due to the lack of nutrients processed by the diseased GI tract.

Crohn’s is categorized into five subtypes, based on the location of the inflammation:

- **Ileocolitis:** This is the most common type, which affects the ileum, occurring in approximately 45 percent of Crohn’s patients.
- **Ileitis:** This type, occurring in approximately 30 percent of Crohn’s patients, also affects the ileum, but it is more severe and can lead to the formation of abscesses or fistulas, or abnormal tubes between the intestines and the abdomen or skin.
- **Granulomatous:** One-fifth of all Crohn’s patients have this type, affecting the main part of the large intestine, including the sigmoid.
- **Gastroduodenal:** This relatively rare type affects the area between the stomach and the small intestine, affecting only about 5 percent of patients.
- **Jejunileitis:** The remaining 5 percent of patients develop this type, which affects the main part of the small intestine.

Crohn’s generally manifests in the late teens or 20s, although it can appear at any age. People of European ancestry are at slightly higher risk, particularly Ashkenazi Jews. It is also more prevalent in developed nations and urban areas.

Roughly 780,000 Americans have Crohn’s at any time, according to the Crohn’s and Colitis Foundation of America. However, a Crohn’s disease information website hosted by AbbVie Inc., a U.S. pharmaceutical firm, puts the number at 700,000, while a 2016 USA Today report cites 570,000. The Centers for Disease Control and Prevention cautions that due to inconsistent definitions and diagnoses, a precise number cannot be known.

Of those with the disease, nearly half are in remission, 30 percent have a mild case, 20 percent have a moderately severe case and 2 percent have a severe case. This will change in each patient, however, and roughly 75 percent of patients with Crohn’s will require surgery at some point in their lives.
Causes of Crohn’s Disease

The cause of Crohn’s is not presently understood. Researchers are looking at a variety of possible causes, ranging from immune system disorders to genetics. It is not currently believed that stress or diet play a role in triggering Crohn’s, although smoking tobacco is associated with both increased risk and severity of disease.

While most people with Crohn’s do not have a family history of it, it is still more prevalent in some families than others, meaning there may be a hereditary predisposition.

Numerous studies are ongoing to try to determine the cause — or, more likely, causes — of Crohn’s. One recent study suggests it may be the result of a specific combination of bacteria and fungi in the digestive tract. Another recent study, built upon earlier studies that looked into genetic links to Crohn’s, found a series of mutations of genes that regulate the body’s ability to react to the presence of bacteria in the digestive tract. It is thought that the inability to recognize these bacteria as normal and necessary may cause the body to react in a way that damages the body itself.

Symptoms and Progression of Crohn’s Disease

The first symptoms of Crohn’s are similar to those of other IBDs and numerous other unrelated GI afflictions.

Diarrhea, cramping, bloating, gas, fever and fatigue are all common symptoms of Crohn’s in its early stages. Those with a more severe case may also exhibit oral ulcers, bloody stool and anal drainage. Depending on the location of the inflammation, patients may experience unexplained and unplanned weight loss due to intestines’ inability to extract nutrients from food.

As the disease progresses, it can lead to GI strictures (which can produce obstructive symptoms such as vomiting, bloating, severe abdominal distress and distension), ulcers or fistulas. In rare cases, the disease’s severity will spread to the skin, blood and even endocrine system (known as extra-intestinal manifestations, or EIMs). Pyoderma gangrenosum, which is associated with Crohn’s (and ulcerative colitis), is a deep skin ulcer often found on the legs. Other EIMs include episcleritis (inflammation of the eye), some types of arthritis and erythema nodosum (red nodules on the skin, usually near the ankles).

If the disease affects the small intestine in those diagnosed before adulthood, the resulting malnutrition will lead to growth retardation or delayed onset of puberty.

In most patients, Crohn’s is marked by long periods of remission, punctuated by periodic flare-ups of varying severity.

Diagnosing Crohn’s Disease

Because of the similarity of Crohn’s symptoms to other GI maladies, and because Crohn’s is a definition based on symptoms, making a specific diagnosis can be challenging. For instance, differentiating between Crohn’s affecting the large intestine and ulcerative colitis can sometimes prove impossible, leading to a diagnosis of indeterminate colitis.

A diagnosis of Crohn’s will most often result from eliminating other possible causes for symptoms experienced by patients. While GI symptoms are similar to those of many other diseases, ranging from indigestion to cancer, the presence of any EIMs alongside diarrhea, cramping, etc., can strongly indicate the possibility of Crohn’s or other IBD.

As other explanations are ruled out and Crohn’s becomes a possible diagnosis, there are a variety of tools available. An endoscopy can be ordered to visually look at the internal damage to the GI tract and take biopsies. Depending on the specific symptoms and results of prior tests, the physician may order a colonoscopy to check the large intestine, an upper GI endoscopy to inspect the stomach and duodenum, or an enteroscopy to look at the small intestine. Biopsies will be examined for the presence of granulomas, which can indicate Crohn’s. If a physician isn’t sure which part of the digestive tract is symptomatic, or if there is a need for a fuller picture of the patient’s GI system, then a capsule endoscopy may be used. A computed tomography scan or magnetic resonance image may also be ordered to look for damage consistent with Crohn’s.

Treating Crohn’s Disease

There is presently no way to prevent Crohn’s, and there is no cure. Treatments vary widely depending on where in the patient’s GI tract it manifests, how severe the case is and the patient’s age and overall health.
While surgery is often necessary to remove strictures or other heavily damaged segments of the intestinal tract, or to repair or remove ulcers, most physicians will begin with a medication regimen and diet and lifestyle changes. The goal of Crohn’s treatment is to induce remission and sustain it as long as possible to reduce the number and severity of flare-ups.\(^2\)

Treatment generally begins with an anti-inflammatory drug to try to control symptoms and, hopefully, promote remission. Anti-inflammatory drugs used to treat Crohn’s fall into two broad categories: aminosalicylates (which have been used to treat Crohn’s disease for more than 30 years) and corticosteroids. Both classes of drugs cause significant side effects, and neither is 100 percent effective at bringing about improvement in all patients. The patient’s history, specifics of the disease and overall health will help the physician devise the best approach.

Aminosalicylates, according to the National Institutes of Health’s National Institute of Diabetes and Digestive and Kidney Diseases, are used by many physicians to treat new, mild cases of Crohn’s. This class of drugs, which is administered orally, includes balsalazide, mesalamine, olsalazine and sulfasalazine.\(^2\) Unfortunately, the side effects are often the same as the symptoms from Crohn’s: diarrhea, vomiting, nausea and abdominal pain. However, some studies indicate that mesalamine can induce remission in about half of patients who receive it.\(^2\)

According to Britain’s National Health Service, corticosteroids are also used first by many doctors.\(^2\) Prednisolone can be taken orally, or hydrocortisone can be given via injection. However, due to the numerous side effects (facial swelling, weight gain, reduced immune response, weakening of the bones), corticosteroids are generally only prescribed for short durations. And, some patients will not respond to corticosteroids.

If anti-inflammatory drugs are not successful, then other, more powerful — and potentially dangerous — drugs may be tried. These include immunosuppressant drugs, TNF inhibitors, ustekinumab, cyclosporine and high-dose immune globulin (IG).

The most widely used immunosuppressant drugs include azathioprine (Imuran) and mercaptopurine (Purinethol).\(^2\) Potential side effects include higher risk of infection and some cancers, as well as inflammation of the liver and pancreas, so they require regular monitoring.

Tumor necrosis factor (TNF) inhibitors are used for moderate to severe cases of Crohn’s. These powerful drugs work by neutralizing the TNF protein in the body’s immune system, and include infliximab (Remicade), adalimumab (Humira) and certolizumab pegol (Cimzia). These drugs cannot be used in any patient with tuberculosis or other serious infections. They have proven effective in helping patients who have developed fistulas as a result of Crohn’s, and they may also help induce remission.\(^2\) Use of these drugs is also tied to an increased risk of certain cancers.

Ustekinumab (Stelara), which inhibits production of interleukin 12 and interleukin 23, has also shown some promise in controlling symptoms of Crohn’s, specifically in patients who show no or only temporary improvement as a result of TNF inhibitors.\(^2\) (Interleukins are a class of cytokines secreted by white blood cells as part of the body’s regulation of its immune system.)

Cyclosporine (Gengraf, Neoral, Sandimmune) and tacrolimus (Astagraf XL, Hecoria) can also be used to treat those with fistulas when other drugs have proved ineffective. Again, the potential side effects are serious: kidney and liver damage, seizures and even potentially lethal infections.\(^2\)

High-dose IG has shown promise in inducing remission. While the data pool is currently small, a 2014 study showed that both intravenous and subcutaneous IG had been used with patients who subsequently entered remission. However, the study’s authors argued that these results warrant further study.\(^2\)

**TREATMENT GENERALLY BEGINS WITH AN ANTI-INFLAMMATORY DRUG TO TRY TO CONTROL SYMPTOMS AND, HOPEFULLY, PROMOTE REMISSION.**

In many cases, other medications — most often, antibiotics and over-the-counter painkillers — are used in combination with one of the above drugs to ameliorate side effects.\(^2\)

There are also other treatment approaches. One is to introduce parasites into the GI tract. A 2015 study that showed the presence of hookworms was associated with a higher incidence of remission suggests the ability of parasites to regulate the body’s immune system to promote their own survival.\(^2\) Another is bowel rest in which patients are put on a liquid diet, intravenous
solution or feeding tube to give the GI tract a few days or longer off to allow inflammation to subside.\textsuperscript{22}

When none of these strategies proves effective, surgery can become unavoidable, with some 75 percent of patients requiring it at some point.\textsuperscript{29} The introduction of laparoscopic surgical techniques has reduced the risks, as well as recovery times and the length of hospitalization, but it is not an option for all procedures. Common surgical interventions will deal with strictures, abscesses or ulcers. In some cases, sections of the intestines or colon are removed if they are too damaged. The most serious cases of Crohn’s can lead to ileostomy, in which the colon and anus are removed, which has serious quality-of-life implications for patients.\textsuperscript{29}

\textbf{Ongoing Research}

There are currently more than 1,000 ongoing clinical studies for Crohn’s disease. The British National Health Service lists 1,356 clinical studies just in the United Kingdom and U.S. as of this writing.\textsuperscript{34} The U.S. federal government’s ClinicalTrials.gov lists 307 (with duplicates between the two lists).

Research into Crohn’s is proceeding on multiple fronts: learning what causes it, finding more effective treatments and searching for a cure. Discovering what causes Crohn’s is most critical because it will obviously allow for more effective and efficient treatments, as well as a clearer path toward an eventual cure.

The Crohn’s and Colitis Foundation of America underwrites the Broad Medical Research Program, which has invested $50 million over the past 15 years into basic research regarding Crohn’s. The foundation aims to raise $2 million per year to put back into primary research. In addition, it is underwriting two other interrelated research programs titled the Genetics Initiative and the Microbiome Initiative. These two programs fund and encourage studies to identify those genes specifically tied to a likelihood of developing Crohn’s, as well as identifying specific bacteria and fungi in the digestive tract. Other initiatives are funding research into pediatric IBD and IBD and pregnancy.

Among the more than 1,300 studies underway in the U.S. and United Kingdom are those to determine the long-term effects and efficacy of dozens of existing medications. Other studies are looking at genetic markers, vitamin supplements to assist juveniles with Crohn’s, using patients’ own fat to grow stem cells to repair fistulas, new surgical techniques to reduce the impact on patients’ quality of life, and new electronic imaging processes to minimize invasive diagnostic testing.

And, there are new medications well into the study pipeline showing real promise:

\begin{itemize}
\item Mongersen is an antisense oligonucleotide that targets SMAD7, a protein involved in the body’s regulatory system. Early results of an ongoing study at the University of California, San Diego, found that some 60 percent of patients who received Mongersen entered remission.\textsuperscript{35}
\end{itemize}
A Finnish study looking at the molecular level of the immune regulatory system suggests that use of the anti-rejection medication daclizumab (Zinbryta) may be useful in treating Crohn’s, as well as multiple sclerosis. There are also some other interesting studies:

• Looking into the interplay between human genes and the naturally occurring microbes that assist with digestion in the GI tract, a 2016 study involving U.S., French and Belgian researchers looked at the population composition of the microbiome (the community of microorganisms naturally occurring in the human digestive tract) of patients with Crohn’s and their family members without Crohn’s. They found a marked difference in the makeup of microbes in those who had Crohn’s versus those who did not. It is not yet known whether this is a result of the changed environment of a GI tract with Crohn’s, or a contributing cause, but it does offer insight into possible treatment options.

• An article in *Nature Immunology* argues that introducing certain beneficial bacteria into the GI tract can help reduce inflammation. Examinations of the microbiome showed that in patients with Crohn’s, the ratio of different species was different than in healthy patients, and by artificially restoring the healthy ratio, inflammation was reduced.

• A study at Arizona State University has identified unique biomarkers that only appear in blood samples of those with Crohn’s, suggesting a one-step blood test for diagnosing is possible.

• An analysis of previous studies suggests that while anti-inflammatory drugs can be effective at relieving symptoms, they do not promote healing of the mucosa layer of the GI tract. On the other hand, several TNF inhibitors — infliximab and adalimumab — have shown promise in promoting healing of the tissue scarred by Crohn’s.

Looking Ahead

As physicians work with their patients to help them maintain as high a quality of life as possible, and to avoid the kinds of life-altering surgical procedures that Crohn’s can require, it is likely that new techniques, drugs and treatments will continue to arrive yearly, if not more often.

Inoculation and/or a cure may be beyond the current horizon, but treatment options that maximize patient quality of life are in the pipeline and on the way.

JIM TRAGESER is a freelance journalist in the San Diego area.
CHRONIC INFLAMMATORY demyelinating polyneuropathy (CIDP) is a type of neuropathy caused by an immune system dysfunction. The true incidence of CIDP is not known since, oftentimes, it is misdiagnosed. People may be diagnosed with CIDP when they don’t have it, or the correct diagnosis of CIDP may be missed. However, it is estimated between five and seven in 100,000 people are affected by it, with approximately 40,000 patients in the U.S. dealing with it at any one time. CIDP can strike any age and gender, although the peak period of development is in the sixth or seventh decade of life, and it affects males more than females. There does not seem to be a genetic link to CIDP.1

What Is CIDP?
CIDP occurs when the immune system malfunctions and creates an antibody that attacks the nerve roots and peripheral nerves resulting in inflammation and damage to the myelin sheath, which covers the nerves and assists in nerve signal transmission. The result is a slowing of the nerve signals and subsequent weakness in the muscles they control. It usually starts in the feet and moves slowly over time up the legs and arms, typically affecting both sides of the body. Both proximal and distal muscles can be involved. Symptoms reported include:3

- Initial limb weakness, both proximal and distal
- Sensory symptoms (e.g., tingling and numbness of hands and feet)
- Motor symptoms (usually predominant)
- Symptoms of autonomic system dysfunction (e.g., orthostatic dizziness)
- Preceding infection (infrequent)
- A relatively acute or subacute onset of symptoms in about 16 percent of patients
- Usually a more precipitous onset of symptoms in children
When the condition is associated with other diseases, symptoms may include:3

- Signs of cranial nerve involvement (e.g., facial muscle paralysis or diplopia)
- Gait abnormalities
- Motor deficits (e.g., symmetric weakness of both proximal and distal muscles in upper and lower extremities)
- Diminished or absent deep tendon reflexes
- Sensory deficits (typically in stocking-glove distribution)
- Impaired coordination

Research is contributing to a greater understanding about this rare neurological disease to help in its diagnosis and develop better treatments.

By Michelle Greer, RN, and Ronale Tucker Rhodes, MS
The rate and severity of progression of weakness varies from person to person; however, CIDP usually presents slowly over several months. This is in contrast to the acute form of demyelinating neuropathy known as Guillain-Barré syndrome (GBS). GBS presents with a rapid progression of symptoms occurring over days or weeks that usually warrants hospitalization due to involvement of the breathing muscles. Respiratory involvement does not occur in CIDP.

**Triggering CIDP**

It is unknown what causes CIDP, but it is believed to be an autoimmune disorder. Autoimmune disorders occur when the body’s natural defenses (antibodies and lymphocytes) against invading organisms suddenly begin to attack perfectly healthy tissue. In the case of CIDP, the autoimmune disorder causes the immune system to attack the myelin cover of the nerves causing inflammation of nerves and nerve roots.

Healthcare providers also consider CIDP as a chronic form of GBS. And, while the specific triggers of CIDP vary, in many cases, the cause cannot be identified.

In addition, CIDP may occur with other conditions such as diabetes (more than half of people with diabetes develop some type of neuropathy), toxins (e.g., heavy metals or chemicals), infections (including certain viral or bacterial infections, Lyme disease, shingles, Epstein-Barr virus, hepatitis C, leprosy, diphtheria and HIV), vitamin deficiencies (B-1, B-6, B-12, E and niacin), physical stress or injury to a nerve (such as from motor vehicle accidents, falls or sports injuries), medications (especially those used to treat cancer), tumors (cancerous and noncancerous growths that develop and press on the nerves), bone marrow disorders (including an abnormal protein in the blood, a form of bone cancer, lymphoma and amyloidosis), other diseases (including kidney disease, liver disease, connective tissue disorders and hypothyroidism) and alcoholism.

**Diagnosing CIDP**

Several years ago, the Peripheral Nerve Society (PNS) and European Federation of Neurological Societies (EFNS) established a task force to create consensus guidelines for diagnosing and managing CIDP. All health plans have medical policies outlining how CIDP therapy will be approved. Many plans base their criteria for approving intravenous immune globulin (IVIG) treatment for CIDP on the PNS/EFNS criteria.

Investigative tests for diagnosing CIDP are presented in Table 1. While there is no single test for a proper diagnosis, neurologists will conduct a thorough history and physical, including a neurological exam, rule out other causes and evaluate the results of electrodiagnostic studies, blood tests and other tests to make an accurate diagnosis. Based on findings, tests will be ordered to further evaluate how the nerves and muscles are functioning. Tests that assist in diagnosing CIDP include:

- Electromyography (EMG), which measures muscle activity to show which muscles and nerves are affected;
- Nerve conduction study (NCS), which measures the speed and efficiency of electrical signals of nerves;
- CSF examination, including cells and protein;
- MRI spinal roots, brachial plexus and lumbosacral plexus;
- Nerve biopsy.

**Table 1. Investigations to Be Considered**

<table>
<thead>
<tr>
<th>For Diagnosing CIDP</th>
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<tbody>
<tr>
<td>Electrodiagnostic studies, including sensory and motor nerve conduction studies, which may be repeated, performed bilaterally or used in proximal stimulation for motor nerves</td>
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<tr>
<td>CSF examination, including cells and protein</td>
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<tr>
<td>MRI spinal roots, brachial plexus and lumbosacral plexus</td>
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<td>Nerve biopsy</td>
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<tr>
<th>For Detecting Concomitant Diseases</th>
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<tbody>
<tr>
<td>Recommended studies:</td>
</tr>
<tr>
<td>Serum and urine paraprotein detection by immunofixation*</td>
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<tr>
<td>Fasting blood glucose</td>
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<tr>
<td>Complete blood count</td>
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<tr>
<td>Renal function</td>
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<tr>
<td>Liver function</td>
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<tr>
<td>Antinuclear factor</td>
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<td>Thyroid function</td>
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<th>Studies to be performed if clinically indicated:</th>
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<tbody>
<tr>
<td>Skeletal survey*</td>
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<tr>
<td>Oral glucose tolerance test</td>
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<tr>
<td>Borrelia burgdorferi serology</td>
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<tr>
<td>C reactive protein</td>
</tr>
<tr>
<td>Extractable nuclear antigen antibodies</td>
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<tr>
<td>Chest radiograph</td>
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<tr>
<td>Angiotensin-converting enzyme</td>
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<td>HIV antibody</td>
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<tr>
<th>For Detecting Hereditary Neuropathy</th>
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<tbody>
<tr>
<td>Examination of parents and siblings</td>
</tr>
<tr>
<td>Appropriate gene testing (especially PMP22 duplication and connexin 32 mutations)</td>
</tr>
<tr>
<td>Nerve biopsy</td>
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* Repeating these should be considered in patients who are or become unresponsive to treatment.
• Lumbar puncture, which taps into the cerebral spinal fluid (CSF) looking for abnormalities that will show the cause of the neuropathy (in CIDP, protein may be high in the CSF); and
• Nerve biopsy, which looks at a section of a nerve to assess the cause of the damage (not typically performed unless the diagnosis is unclear).

Treating CIDP

The primary goals for treatment of CIDP are to reduce symptoms, improve functional status and, if possible, maintain long-term remission. Therapies that have proved to successfully treat CIDP include corticosteroids, intravenous immune globulin (IVIG), subcutaneous immune globulin (SCIG), plasma exchange (PE) and physiotherapy. Other therapies that have been tried but are not as effective include immunosuppressive agents. Most patients see improvement using these treatment options alone or in combination. In addition, hematopoietic stem cell transplantation (HSCT) is being looked at to put CIDP in remission. Table 2 lists therapies for CIDP.

Corticosteroids have been commonly used to treat CIDP for many years. Initial treatment with oral prednisone is typically high dose at 60 mg to 100 mg per day and then tapered once the patient is stabilized. Unfortunately, there is no strong evidence from randomized controlled trials that corticosteroids are effective, and they cause many undesirable side effects. As a result, several trials have been conducted to evaluate alternative dosing regimens with no difference in efficacy.8,9

Over the last 15 years, IVIG has been considered first-line treatment for CIDP with fewer side effects than corticosteroids. IG therapy protects the nerves in the body from being attacked. IVIG brands that have a U.S. Food and Drug Administration (FDA)-approved indication for CIDP include Gamunex-C (Grifols), Gammaked (Kedrion) and, most recently, Privigen (CSL Behring). The approvals for Gamunex-C and Gammaked were based on the Phase III ICE (IVIG in CIDP Efficacy) trial conducted by Talecris (now Grifols).10 The approval of Privigen was based on the Phase III PRIMA (Privigen Impact on Mobility and Autonomy) and PATH (Polyneuropathy and Treatment with Hizentra) studies conducted by CSL Behring, which showed a 61 percent and 73 percent response rate, respectively (see CSL Behring’s Privigen Approved to Treat CIDP on page 12).11

SCIG therapy is also sometimes used as a successful off-label (not FDA-approved) indication to treat CIDP. Recently, CSL Behring, manufacturer of the SCIG product Hizentra, completed the PATH study, the largest CIDP trial designed to demonstrate the efficacy, safety and tolerability of two different doses of

<table>
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<tr>
<th>Table 2. Therapy for CIDP</th>
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<tr>
<td><strong>Proven therapies from randomized controlled trials:</strong></td>
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<tr>
<td>Level I evidence</td>
</tr>
<tr>
<td>Intravenous immune globulin</td>
</tr>
<tr>
<td>Prednisone</td>
</tr>
<tr>
<td>Plasma exchange</td>
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<tr>
<td>Pulse oral dexamethasone</td>
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</table>

| **Therapies ineffective based upon randomized controlled trials:** |
| Level I evidence; These studies all had difficulties in trial design |
| Azathioprine |
| Interferon B1a (Level II evidence) |
| Methotrexate |

| **Therapies of unproven benefit but probably helpful as steroid-sparing agents, based upon clinical experience and > 1 case series: Level IV evidence** |
| Cyclosporine A |
| Cyclophosphamide |
| Azathioprine |

| **Other therapies of unproven benefit: Level IV evidence** |
| Mycophenolate mofetil |
| Pulse weekly oral prednisolone |
| Pulse weekly oral dexamethasone |
| Pulse weekly intravenous methylprednisolone |
| Rituximab |
| Interferon alpha 2a |
| Etanercept |
| Tacrolimus |
| Alemtuzumab |
| Natalizumab |
| Hematopoietic stem cell transplantation |

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Hizentra, compared with placebo (Privigen), in the maintenance treatment of CIDP patients previously treated with IVIG.12 Study results have not yet been published; however, in July, FDA accepted for review the company’s supplemental biologics license application for Hizentra for the treatment of CIDP as maintenance therapy to prevent relapse of neuromuscular disability and impairment.13 In addition, Shire is currently investigating its SCIG product HyQvia in two Phase III studies for treating CIDP. One is measuring the long-term tolerability and
safety of HyQvia.\textsuperscript{14} The other study is testing the efficacy, safety and tolerability of HyQvia and Gammagard Liquid, the latter of which can be infused through both the IV and SC route.\textsuperscript{15}

Two randomized controlled trials have shown PE to be beneficial in CIDP patients. PE, a process of replacing the plasma in a patient’s blood, begins by withdrawing blood from the patient, removing plasma from the blood, and exchanging it with red blood cells reinfused in a plasma substitute (usually human albumin and saline). The result is proteins located in plasma that are responsible for attacking the nerves are removed from the blood. PE is more time-consuming and invasive than IVIG. And, while improvement in disability and nerve conduction after treatment can be rapid, it is also short-term, and patients often relapse after stopping PE. As such, PE is restricted to second-line treatment in most cases.\textsuperscript{8,9}

Physiotherapy can also play an important role in the assessment and management of CIDP, especially helping to maximize a patient’s physical potential. The goals of physical therapy are to:\textsuperscript{16}

- Maximize muscle strength and minimize muscle wastage by exercise using strengthening techniques;
- Minimize the development of contractures (stiffness) around joints;
- Facilitate mobility and function; and
- Provide a physical assessment that may help in planning future management.

Currently, there is one clinical trial being conducted to determine the effect of resistance and aerobic exercise in CIDP and multifocal motor neuropathy (MMN). The study’s aim is to evaluate changes in muscle strength during high-intensive resistance training and changes in maximal oxygen consumption (\(\text{VO}_2\text{-max}\)) during high-intensive aerobic training in patients with CIDP and MMN in maintenance therapy with SCIG. The hypotheses are that muscle strength and \(\text{VO}_2\text{-max}\) are significantly increased during training sessions.\textsuperscript{27}

Because 25 percent of patients fail to respond or do not respond adequately to corticosteroids, PE and IVIG, and the likelihood of progression of the disease is high, immunosuppressants designed to weaken the immune system so it doesn’t attack the nerves are considered in CIDP patients. These drugs, which are not approved by FDA to treat CIDP, include rituximab (Rituxan), mycophenolate mofetil (Cellcept), azathioprine (Imuran) and methotrexate (Rheumatrex, Trexall, Otrexup, Rasuvo).

Rituximab is a monoclonal antibody that targets a certain portion of B cells, including those that play a role in the immune response thought to occur in autoimmune conditions. Rituximab has been used in several autoimmune neurological conditions, including CIDP. In one multicenter study of 13 CIDP patients who were partial or nonresponders to conventional therapy, nine improved clinically or maintained the improvement seen with IVIG/PE after a median time of two months following the course of rituximab, and the effect lasted for up to one year. In another similar study of 18 patients, six responded to rituximab, showing at least a 1-point improvement on the Rankin scale (commonly used for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability). In addition, a number of case studies have reported on the efficacy of rituximab treatment in CIDP when there is a coexistent B cell disease such as idiopathic thrombocytopenic purpura, SLE\textsuperscript{75} and Morvan syndrome, and myasthenia gravis. However, so far, a significant treatment effect has not been proven.\textsuperscript{8,9}

**THE PRIMARY GOALS FOR TREATMENT OF CIDP ARE TO REDUCE SYMPTOMS, IMPROVE FUNCTIONAL STATUS AND, IF POSSIBLE, MAINTAIN LONG-TERM REMISSION.**

Mycophenolate mofetil (MMF) inhibits white blood cell proliferation and formation of adhesion molecules (that play a major role in the recruitment of neutrophils to the site of inflammation) and migration.\textsuperscript{18} In a study, researchers analyzed a database of 184 patients with CIDP to obtain clinical, laboratory and electrophysiological information for patients with CIDP treated with MMF. Eight patients who met the inclusion criteria received 2 grams of MMF per day for a median duration of 15.2 months. The average Neuropathy Impairment Score of those patients improved from baseline (72.3±35) to after initiation of MMF therapy (37.8±37). Six patients were either able to stop concomitant medications (corticosteroids, IVIG) or reduce their doses and frequency by equal to or greater than 50 percent.\textsuperscript{19} Currently, a Phase III clinical trial is ongoing to investigate if MMF could decrease the proportion of patients who relapse during the IVIG tapering period after IVIG withdrawal.\textsuperscript{20}
Proven **safe.** Proven **effective.**
And the only IVIg **stabilized** with proline.

**Important Safety Information**
Privigen is approved to:
- Treat types of primary immunodeficiency (PI).
- Raise platelet counts in patients over 15 with chronic immune thrombocytopenic purpura (ITP).
- Treat chronic inflammatory demyelinating polyneuropathy (CIDP) in adults. Talk with your doctor about the length of your therapy.

Please see the brief summary of prescribing information on the following page.
Important Safety Information

WARNINGS:

- Thrombosis (blood clotting) can occur with immune globulin products, including Privigen. Risk factors may include advanced age, prolonged immobilization, a history of blood clotting or hyperviscosity (thick blood), use of estrogens, installed vascular catheters, and cardiovascular risk factors.
- In predisposed patients, kidney malfunction and acute kidney failure, potentially fatal, can occur with the administration of human immune globulin intravenous (IGIV) products. Kidney problems occur more commonly in patients receiving IGIV products that contain sucrose. Privigen does not contain sucrose.
- If you are at high risk of thrombosis or kidney problems, your doctor will prescribe and administer Privigen at the minimum dose and infusion rate practicable, and will monitor you for signs and symptoms of thrombosis and viscosity, as well as kidney function. Always drink sufficient fluids before administration.

See your doctor for a full explanation, and the full prescribing information for complete boxed warning.

Treatment with Privigen might not be possible if your doctor determines you have hyperprolinemia (too much proline in the blood) or are IgA-deficient with antibodies to IgA and a history of hypersensitivity. Tell your doctor if you have previously had a severe allergic reaction (including anaphylaxis) to the administration of human immune globulin. Inform your physician if you notice early signs of hypersensitivity reactions to administration of Privigen, including hives, tightness of the chest, wheezing, or shock.

Immediately report to your physician the following symptoms, which could be signs of serious adverse reactions to Privigen:

- Pain and/or swelling or discoloration of an arm or leg, shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, and numbness or weakness on one side of the body (possible symptoms of a blood clot).
- Headache; a stiff neck; excessive drowsiness or fatigue; fever; sensitivity to light or painful eye movements; nausea; increased heart rate; yellowing of the skin or eyes, and/or dark-colored urine (possible symptoms of other conditions that may require treatment).

Privigen is made from human blood. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent and its variant (vCJD), cannot be completely eliminated.

Before receiving any vaccine, tell the immunizing physician if you have had recent therapy with Privigen, as the effectiveness of the vaccine could be compromised.

In clinical trials of Privigen, headache was the most common side effect seen in all conditions treated (PI, ITP, and CIDP). Other common side effects that can be seen with treatment include fatigue, nausea, fever, and high blood pressure. These are not the only side effects possible; see the full prescribing information for a complete list of adverse reactions possible with treatment for each condition. Alert your physician to any side effect that bothers you or does not go away.

Please see the following brief summary of prescribing information for Privigen, including boxed warning.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.

Call for support 1-877-355-IGIQ (4447)
Monday–Friday, 8 AM to 8 PM ET

IgIQ is ready to help

All the support you need. All in the same place.

For people taking Privigen, CSL Behring offers a comprehensive set of services to help make Ig therapy accessible and affordable. IgIQ provides:
- Financial assistance
- Patient support
- Insurance navigation
- Referral triage
- General information

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Privigen safely and effectively. See full prescribing information for Privigen.

Privigen® Immune Globulin Intravenous (Human), 10% Liquid

Initial U.S. Approval: 2007

WARNING: THROMBOSIS, RENAL DYSFUNCTION AND ACUTE RENAL FAILURE

See full prescribing information for complete boxed warning.

- Thrombosis may occur with immune globulin products, including Privigen. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors.
- Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IGIV) products in predisposed patients. Renal dysfunction and acute renal failure occur more commonly in patients receiving IGIV products containing sucrose. Privigen does not contain sucrose.
- For patients at risk of thrombosis, renal dysfunction or failure, administer Privigen at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

INDICATIONS AND USAGE

See full prescribing information for complete boxed warning.

- Primary humoral immunodeficiency (PI)
- Chronic immune thrombocytopenic purpura (ITP) in patients age 15 years and older
- Chronic inflammatory demyelinating polyneuropathy (CIDP) in adults

Limitations of Use:

- Privigen maintenance therapy in CIDP has not been studied beyond 6 months.

CONTRAINDICATIONS

- History of anaphylactic or severe systemic reaction to human immune globulin
- Hyperprolinaemia (Privigen contains the stabilizer L-proline)
- IgA-deficient patients with antibodies to IgA and a history of hypersensitivity

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- IgA-deficient patients with antibodies to IgA and a history of hypersensitivity

ADVERSE REACTIONS

- The most common adverse reactions, observed in >5% of study subjects, were headache, fatigue, nausea, chills, vomiting, back pain, pain, elevated body temperature, abdominal pain, diarrhea, cough, stomach discomfort, chest pain, joint swelling/effusion, influenza-like illness, pharyngolaryngeal pain, urticaria, and dizziness. Serious adverse reactions were hemolysis, exacerbation of CIDP, acute kidney injury, or volume overload.
- The most common adverse reactions in patients at increased risk of thrombosis, hemolysis, acute kidney injury, or volume overload.

DRUG INTERACTIONS

- The passive transfer of antibodies may:
  - Lead to misinterpretation of the results of serological testing.
  - Interfere with the response to live virus vaccines.

USE IN SPECIFIC POPULATIONS

- Geriatric: In patients over age 65 or in any patient at risk of developing renal insufficiency, do not exceed the recommended dose, and infuse Privigen at the minimum rate practicable.

See 17 for PATIENT COUNSELING INFORMATION.

Based on September 2017 revision
Azathioprine is controversial in treating CIDP. In some small cases studies, azathioprine in combination with glucocorticoid therapy at higher doses led to improvement. Methotrexate has been studied in patients with CIDP with no significant results. In one study, 60 patients were enrolled in a multicenter trial to receive either a placebo or methotrexate, all of whom were co-treated with glucocorticoids or IVIG. The primary endpoint was a 20 percent reduction in mean weekly dose of either glucocorticoids or IVIG by the end of the trial, but findings showed no significant difference in the primary outcome between the methotrexate and placebo groups. In another multicenter study, researchers compared 60 CIDP patients requiring corticosteroids or IVIG, 27 of whom were prescribed oral methotrexate and 32 of whom were given a placebo. Primary outcome was a greater than 20 percent reduction in mean weekly dose in the last four weeks of the trial compared with the first four weeks. Secondary outcomes analyzed separately at mid-trial and final visits measured activity limitations and strength. Forty-five (52 percent) taking methotrexate and 14 (44 percent) taking a placebo had a greater than 20 percent reduction in mean weekly dose of corticosteroids or IVIG. However, there were no clinically and statistically significant differences in secondary outcomes. Lastly, limited HSCTs have been performed in refractory CIDP patients. In one small, uncontrolled trial, autologous HSCT (AH SCT) was performed in 11 consecutive patients with CIDP refractory to first-line immunomodulatory treatments and one or more second-line treatments. The total median Inflammatory Neuropathy Cause and Treatment and Rankin scores improved significantly within two months to six months after AH SCT. Eight of the 11 patients maintained drug-free remission, with three of the 11 relapsed during the follow-up period, requiring retransplantation with AH SCT in one. Complications occurred following six of the transplantations, but resolved spontaneously or with treatment. The authors concluded that “AH SCT can be efficacious in therapy-refractory CIDP, with a manageable complication profile, although randomized controlled trials are needed.”

Currently, a Phase II study is being conducted to examine whether treating patients with high-dose cyclophosphamide (a drug that reduces the function of the immune system) and ATG (an immunosuppressive agent that selectively destroys T lymphocytes), followed by return of the previously collected blood stem cells, will stop the progression of CIDP. The purpose is to evaluate whether this treatment will produce a normal immune system that will no longer attack the body.

A Rare, Complicated Disease
CIDP is a rare, complicated disease that has many different causes, with a great deal of variability in symptoms from patient to patient. Much research is being conducted to advance scientific understanding of the underlying pathogenesis of CIDP, homing in on diagnostic criteria and establishing optimum treatment doses and durations for established therapies, as well as to further investigate alternative, less-well studied treatments. For now, many therapies have proven successful in managing the symptoms in CIDP patients. But, it is hoped that in the future, more effective therapies and, perhaps, even a cure may be available.

MICHELLE GREER, RN, is senior vice president of sales for NuFACTOR Specialty Pharmacy. RONALE TUCKER RHODES, MS, is the editor in chief for IG Living magazine.

References
A MATTER OF LIFE OR DEBT

While the future of healthcare in this country remains in limbo, the troubling reality is that even those who currently have health insurance simply can’t afford to get sick.

By Trudie Mitschang
STATISTICS SHOW that individuals juggling unpaid medical bills have ample company. According to a 2016 report, more than a quarter of Americans say someone in their household is struggling to pay a medical debt.¹ The reasons for this rising tide of unpaid healthcare costs are varied; some are dealing with unrelenting costs associated with managing a chronic illness, while still others have simply been sidelined by a sudden, unexpected injury or diagnosis. And, for a large number of American families, mounting medical debt can lead to financial ruin. Currently, medical debt is the No. 1 cause of personal bankruptcy in the U.S. Even more troubling is, oftentimes, the most tragic losses occur for those who have health insurance. One Consumer Reports study found 30 percent of Americans with private health insurance have received unexpected bills following procedures they thought were covered. Of those, 23 percent received a bill from a doctor they didn’t expect to get a bill from. And, 14 percent said they were charged higher out-of-network rates by doctors they thought were in-network.²

“I was admitted January 2016 to a participating hospital for pleurisy,” recalls Julie Claire, a 59-year-old from Michigan. “I spent eight days on IV antibiotics until the surgeon insisted that a video-assisted procedure needed to be performed. During the course of that procedure, the mess that he encountered, both inside and outside my lung, caused him to perform an unscheduled thoracotomy. The surgeon did not participate with my insurance, but he was the only surgeon qualified to perform this procedure. I have two deductibles to pay and copayments for each plan. My surgeon’s bill alone was $10,400.”²

Understanding the Cost of Chronic Disease

From copayments and out-of-network costs, to insurance claim denials and appeals and the loss of wages due to disability, expenses linked to chronic illness can quickly balloon out of control. Add to that the complexity of chronic illness and the fallout from medication side effects, and it’s easy to see how bills pile up. For example, many patients with Crohn’s disease develop secondary autoimmune diseases such as rheumatoid arthritis, lupus and fibromyalgia, sending them on a complex journey through the healthcare system. A patient in this scenario is likely to incur overlapping expenses for each diagnosis and treatment plan, while still trying to address the original illness. Additionally, drug side effects can create serious and expensive medical problems such as the need for hip replacements that are often linked to prednisone use, or repeated hospitalizations from infections linked to immunosuppressant drugs.

Of course, medical bills are not the only factor when it comes to mounting debt; the very nature of many chronic diseases prevents patients from consistently working and earning a living. This lack of cash flow combined with accumulating medical debt can damage credit ratings, lead to harassing debt collection calls and add undue stress at a time when all mental and emotional resources are needed to simply stay on top of the disease itself. Patients often describe this scenario as adding “insult to injury.”

CURRENTLY, MEDICAL DEBT IS THE NO. 1 CAUSE OF PERSONAL BANKRUPTCY IN THE U.S.

Like other types of debt, medical debt tends to accumulate over time, especially for patients who require daily medications or ongoing care. Lene Anderson, who was diagnosed with juvenile arthritis at age 4, has used a power wheelchair since her teens and is well-versed in managing the high costs of chronic illness. Anderson makes her living as a writer and chronic illness advocate and is the author of the award-winning blog The Seated View. But, not so long ago, Anderson watched helplessly as her own slow creep into medical debt pushed her to the brink of bankruptcy. “For a long time, my medications and the costs incurred with my disability (wheelchair repair, etc.) had been accumulating,” she explained. “Every month, the debt ratcheted up a bit more, and every month, I tried to pay off as much as I could. I reached a point when the minimum payments were so significant that I never paid off any of the principal, and when paying that minimum put me so far behind that I had to use credit to buy medication. It was a vicious cycle. Five years ago, I found myself paying off one credit card with another, and I knew it was time to face facts and do something drastic about it.”

For Anderson, taking back control began with seeking credit counseling and considering all of her options, including bankruptcy. “For a number of reasons, declaring bankruptcy was not the ideal solution for me, so I ended up with a debt settlement plan,” she said.

TACTICS TO HELP BEAT THE ODDS

Financial experts and patient advocates agree that mounting medical debt is a widespread problem for millions, with no
simple solution. While each patient’s scenario is unique, individuals can take a number of practical steps if they find themselves overwhelmed by accumulating bills. Laurie Miller, a registered nurse and patient with chronic illness, advises the following:

• Check your medical bills thoroughly. Hospitals and clinics bill insurance and patients based on a diagnosis code or procedure code. This means they bill for an estimated cost of the entire procedure rather than the actual procedural costs, including the cost of paying medical professionals, use of facility equipment and the number of supplies used during a procedure. It is possible that you are being charged for items or services you don’t actually need, so ask for itemized statements. If you were billed for a particular item or service you did not use, it can be removed from the bill, or the amount can be refunded to you if payment was already received.
• Be proactive; ignoring medical bills will not make them go away. When you are sick and have to go to numerous providers, as well as experience numerous hospital stays, the piles of medical bills can be enormous. You will get one from every doctor and service provider, as well as from every laboratory and radiological facility. You will also usually be billed separately for emergency physicians and anesthesiologists. Often, if you initiate contact with the hospital business office, the staff may be willing to work with you, offer financial aid and/or set up a plan with payments that are within your means. Explain your financial situation to them, including your income and the number of medical bills you have incurred. Ask if you qualify for financial assistance, which will enable you to pay less for each bill. Just don’t wait until bills are past due to explore your options.
• Ask for combined accounts to streamline payments. Oftentimes, medical bills have different account numbers for every clinic visit and every hospital visit. It is usually possible to combine those account numbers so you will only have one clinic bill payment and one hospital bill payment, but you will probably need to ask the business office staff to do this for you. The benefit of this is that you will have one hospital/clinic payment rather than five payments going to five different account numbers at the same hospital/clinic. You will usually need to deal with the hospital business office and clinic business office staff separately.
• Don’t take out a loan or second mortgage to pay off medical bills. While hospitals and health systems will often work with you to pay for your healthcare costs, most banks do not. You don’t want to lose your home while trying to pay off medical bills. Remember, if you still owe money to the bank for your home, including a second mortgage or line of credit, the bank owns your home and can repossess it at any time if payments should stop. If you must, consider refinancing your home instead so your monthly mortgage payment is less. This may then enable you to contribute more toward your medical bills.

As Anderson discovered when her debt load exceeded her ability to pay, contacting reputable credit counseling services can offer much-needed relief, especially if other options to negotiate the debt are unsuccessful. These types of services are often free and can offer assistance with setting financial goals, planning a working budget and paying down debt. Sometimes, a credit counselor will arrange to receive one payment from an individual and then pay individual bills for him or her. While this may seem humiliating, it can also greatly reduce stress.

Helpful Resources

• Patient Advocate Foundation (PAF) (www.patientadvocate.org) offers a range of services for patients facing medical debt crisis issues, including referrals to charity care and assistance with setting up payment plans. If a patient has a diagnosis that qualifies for copay assistance, the patient may be referred to PAF’s Co-Pay Relief Program to determine program eligibility.

• Needy Meds (800-503-6897, www.needymeds.org) provides a prescription savings card that enables those eligible to get discounts on certain medications at participating pharmacies throughout the nation.

• RxAssist.org offers a database of drug assistance programs provided by pharmaceutical companies that enable patients to receive assistance with numerous medications.

• The Partnership for Prescription Assistance (www.pparx.org) also helps people find prescription assistance programs, as well as free or low-cost healthcare clinics.

• Medicare Rights Center Hotline (800-333-4114) is available to seniors or individuals with a disability. When using the service, callers can learn about Medicare and other resources available to them for obtaining public health insurance. The hotline also offers assistance for dealing with medical bills.
Shaking Off the Shame

The financial consequences of skyrocketing medical debt are easy to calculate. What is less obvious is the heavy emotional toll associated with unpaid bills. Illogical as it may seem, many people feel intense shame when it comes to medical debt, an emotionally toxic situation that can lead to even further declines in health. In an effort to avoid getting deeper in debt, some patients may stop seeking medical care altogether. A study in the Journal of General Internal Medicine showed that over two-thirds of those who either had current medical debt or had been referred to a collection agency reported it caused them to seek alternative sites of care or to delay or avoid seeking subsequent care when needed.3

In a nutshell, patients who can’t afford to pay are less likely to seek care because they are ashamed about their debt and don’t want to end up owing more. Still, as Anderson learned, confronting the problem on can be an important first step in getting the help needed to recover mentally, emotionally and financially. “It’s important to remember there is no shame in not being able to stay ahead of a debt that’s incurred simply because you’re sick. It’s not like you’re going out clubbing every night, putting champagne on your cereal and have a gold Ferrari in the garage,” she says. “The money is going to medication, doctor’s appointments and the tests you need to stay ahead of your condition.”

New Reporting Standards Offer Collection Agency Reprieve

When you are ill, the effects of medical debt on your FICO score may seem like the least of your concerns. But unpaid accounts that go to collections can haunt people for years, limiting their ability to qualify for a home or car loan or obtain other types of credit in the future. According to a 2014 report by the Federal Consumer Financial Protection Bureau, as many as 43 million Americans have medical debt in collections that has adversely affected their credit. The study also found that for 15 million consumers, medical debt was the only blemish on their credit report. In an effort to address this issue, the three major credit reporting agencies — Experian, Equifax and TransUnion — have established a 180-day waiting period before including medical debt on a consumer’s credit report. The policy went into effect in late 2017, and the new six-month period is intended to provide enough time for individuals to resolve disputes with insurers and delays in payment before their credit score takes an unnecessary hit.

Remain Proactive to Get Back on Track

Without question, navigating a maze of medical debt can make it feel as if the odds — and the bills — are stacked against a person. From an unexpected emergency room visit or the loss of a job that provided health insurance, to the long-term costs of a chronic condition, medical debt is a daily reality for one in five Americans. For those affected, digging themselves out can seem daunting or even impossible. The good news is options and resources are available, as long as individuals remain proactive and seek help while negotiation is still possible. “Don’t lie to yourself,” says Anderson. “I should have faced facts a couple of years before I did, but I kept telling myself that I could absolutely make a dent in my debt. This was a complete delusion. In the end, a negotiation with my creditors led to me committing to pay back part of my debts, and after five years, I have just finished that process. This situation allowed me to get a handle on my finances and even build up my savings again.”

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.

References
JAMIE STEWART is a former IG Living blogger and chronic inflammatory demyelinating polyneuropathy (CIDP) patient who has faced numerous health setbacks over the years, including a failed stem cell transplant. Following the loss of his marriage and subsequent battle with depression, Jamie has learned to appreciate his own resilience and hopes to help other patients to do the same.

Trudie: Tell us about your first diagnosis.
Jamie: In November 2010, I received the H1N1 [influenza] vaccine. Shortly thereafter, I experienced severe nerve pain in my thighs and slowly started losing muscle strength. Symptoms continued to degrade, and approximately 18 months later, I was officially diagnosed with atypical CIDP. I initially tried high-dose prednisone with no luck. I was then treated with intravenous immune globulin (IVIG), but the dosing levels were incorrect. As I continued to get sicker, I sought a stem cell transplant to hopefully stop the disease progression. My goal was simple: stop the disease, keep my job and restore my quality of life. I was accepted by three highly accredited international stem cell transplant centers and chose Moscow, Russia, because that center had the most experience with this type of procedure.

Trudie: What was it like to undergo a stem cell transplant?
Jamie: The transplant itself was pretty much insignificant. I had a few minor issues, but all were quickly resolved by the medical staff. Upon returning home, I was to wait six months and have a lumbar puncture to determine if the stem cell transplant was a success. Unfortunately, my inflammatory markers did not improve, and the transplant was a failure. I knew going in that this was a possibility. Data show that stem cell transplantation is about 80 percent successful for multiple sclerosis, but data was not available for CIDP patients, as it was too new.

Trudie: When you first blogged for us, you were married. Tell us how your illness affected your relationship with your wife.
Jamie: Chronic illness is hard on a marriage, very hard. Roles change within the marriage. Things get taken for granted, communication breaks down and, eventually, walls get built up. It didn’t help that neither of our families took an active role in assisting us as we went through this. I don’t think people can fully understand the stress that comes with a rare disease. Not only were we trying to understand what was happening to my body, but we were constantly having to fight with doctors, insurance companies and the supposed friends who thought I was faking.

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There are only a few places a person can turn to for help. I live in a small community, and there are no advocacy programs available, at least none for CIDP. I did reach out to national
organizations, but none had advocates in my area. *IG Living* was the only organization that truly assisted.

My ex and I had talked numerous times about how the stress was affecting each of us. I was aware that I needed to talk with a mental health provider, someone I could go to blow off steam when I felt overwhelmed. I encouraged her to do the same. No one tells you what to expect when dealing with CIDP. We didn’t know that at times my skin would be so sensitive that taking a shower would be painful. No one told us that with the increased pain and fatigue, intimacy would become an issue. Patience and understanding were eroded as we communicated less and less.

**Trudie:** What happened when you returned from Moscow?

**Jamie:** I knew before I left for Moscow that things were not good in our marriage. By this time, I alternated between barely being able to work and being bedridden. My ex had become so depressed that she wouldn’t leave the house except to go to work. I did implore her to see a counselor, but she refused. The last straw was the day she called me a burden.

**Trudie:** Your health took a turn for the worst shortly after your marriage ended. What happened?

**Jamie:** I kept having horrible bouts of fatigue accompanied with upper-respiratory issues. I knew that I was IgA- and IgM-deficient; I was told this can happen after receiving chemotherapy. I also knew I was under immense stress with the divorce and everything else in my life. When it felt like my blood was stopping, I knew I needed to see a doctor. After a few tests, I learned that I have secondary adrenal insufficiency, low testosterone and probable common variable immunodeficiency. It was a good thing I got tested. My cortisol levels were so low that I had become disoriented. I was on the verge of a full-blown adrenal crisis, which can result in death. It was not a great way to begin your newly single life.

**Trudie:** What is your current medication/treatment plan?

**Jamie:** I am on many medications: IVIG 40 grams every other week, daily testosterone gel, hydrocortisone replacement, narcotic pain medications, pregabaline, tizanidine, Ambien and a statin for high cholesterol. I will probably need to add an antibiotic to keep the upper-respiratory issues under control. I use a steroid inhaler and have an oxygen concentrator for when I sleep. Even with all these setbacks, the plan is to improve my quality of life. My goal is simple: to be able to enjoy life to the fullest. I want to travel more often. I still volunteer and am an advocate for rare diseases.

**Trudie:** What lessons have you learned from all of this?

**Jamie:** I have learned that I am my best advocate. Doctors can be challenged, and when a doctor is unwilling to work with you, then it’s time to fire the doctor and find a new one. Don’t waste your time and energy on trying to change a doctor’s mind. Also, a rare, chronic illness is unbelievably stressful. I would suggest anyone diagnosed seek out a mental health professional. Mental health is so important, but is rarely discussed. The circle of support will be small, if any. I had to learn that if I had cancer, I would have received a tremendous amount of support and help, but when people don’t understand what you have, they really don’t know how to engage.

**Trudie:** How do you stay positive in the face of so many challenges?

**Jamie:** Living in the moment has really helped me to stay grounded. I realize that things will usually get better, no matter the circumstance. This realization came after my adrenal crisis. I take enjoyment in the things that I lost the ability to do, but have regained — like taking my dogs for walks. I allow myself to have “pity parties,” but they can only last one day. If after one day I am still feeling down, I seek out my mental health doctor. New hobbies have also helped me to feel good about myself again. I am learning to draw and paint, both very poorly, but it is fun!

**Trudie Mitschang** is a contributing writer for *IG Living* magazine.
**It Was Enough**

By Stacey Philpot

Perhaps, like me, you sometimes lie awake at night. Instead of counting sheep, you count your failures or your inadequacies. You recount each “if only,” “I should have” and “I’m not enough” that the day has revealed within you. Did you miss an important event at work or in the life of someone you love because of your illness? Strike one. Did you have to rest instead of loading the dishwasher or making that phone call as you’d intended? Strike two. Did you struggle to get out of bed today, marking not a single item off of your to-do list? Strike three. Unlike baseball, there isn’t a merciful “Out!” from the umpire so you can try again next time. The strike count just keeps growing day by endless day.

Will you ever be enough?

I remember when my daughter was about 2 years old and still blessing me by taking afternoon naps. On one particular day, I’d struggled greatly to get up the stairs to lay her down for her nap. By the time we got to her room, not only was I in tremendous pain, I was having an asthma attack. She took her time, carefully selecting the three books I was to read to her before she went to sleep, as our daily routine dictated. Silently, I begged her to choose one-word books and to fall asleep after the first. I had no idea how I’d make it through three stories. Naturally, she chose the three longest books she owned and spent the next seven minutes arranging her blankets and animals just so before I could begin reading. I thought I might actually fall over. Instead, I sat on the side of her bed and began panting and reading. At the end of the second book, I closed it, placed the stack of books on the floor, kissed her head, and told her, “That’s all Mommy can read today. I love you so much. Get good sleep now.” She immediately began to cry. She was tired and had been short-changed on her book time.

I closed her door and immediately began to cry. I struggled down the stairs while berating myself for not being able to read my own child another story. At the bottom of the stairs, I had a strange epiphany. Suddenly it was clear: I always saw what I hadn’t done, the stories I hadn’t read. I never credited myself for what I had done, the stories I had read. I was measuring myself against an impossible standard, one where I would always come up lacking. I was comparing myself to an able-bodied person.

I realized that day that I had to reframe my thought process. Instead of comparing myself to an able-bodied person and shaming myself for failing to do what he or she might have accomplished, I had to ask myself: “Have I given my all?” If the answer was yes, then it was enough, whatever “it” was.

Did you offer your all today? If you did, it was enough.

Sometimes “all” is difficult to define. How do we know when we’ve given our all? Especially when it changes daily? We know “all” will be individual and ever-changing. One day, giving my all may mean taking care of my body by obtaining the treatments it requires. On another, giving my all may mean 15 minutes of time on the floor playing Barbies, offering my full attention to my daughter.

Giving our all may include a myriad of things like loving, sacrificing, self-care, finding ways to chase our dreams or enjoying the things we love. It’s true we may not be able to offer ourselves to some pursuits (like mountain biking or skydiving), but if we’re offering all we have, what more can anyone ask of us? What more can we ask of ourselves? In fact, like rare gemstones, don’t our offerings become more, not less, valuable?

Did you give your all today? If so, it was enough.

Did you offer your all today? If you did, it was enough.

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Stacey Philpot

Stacey Philpot is an author, gooball and avid reader. You can find her blog at chronically whole.com, where she shares her journey of making the most of a life touched by common variable immunodeficiency, Lyme disease and rheumatoid arthritis.
There’s no shortage of chronic illness patients who are willing to share their real lives on Instagram. There are hashtags for every disease under the sun — even #HospitalGlam for girls looking to prove that even on their worst day, they can still be beautiful. Even so, most of the feed is probably filled with celebrities, old friends from high school and girls who’ve had tummy tucks trying to sell waist trainers.

I try to keep a good balance in my social media accounts from “I’m someone with a chronic disease that affects every moment of my life” to “I’m someone with a job, a husband and a dog, who is addicted to the thrill of finding a sundress under $11, and who likes to take pictures of food that show I have zero self-control when it comes to portion size.”

This summer, I saw pictures on my feed from people my age who were backpacking across Europe, lying on the beach, going to theme parks and knocking back piña coladas like it was their full-time job. All while I sat on my bed, anchored to my IV pole, knowing there wasn’t a bandage that would fully cover my accessed port well enough to go for a swim. I laid there, exhausted from just carrying my groceries from my car to my front door, knowing I definitely couldn’t hack carrying an overstuffed backpack through Amsterdam.

I tried not to let that completely sour feeling of jealousy sweep over me every time I scrolled through my feed. To be honest, half of the things these people were posting weren’t even things I had any personal desire to do. I didn’t want to jump off a waterfall or go to an Incubus concert. I didn’t want to bleach my hair and then dye it hot pink. I just wanted to feel like I could do these things, if I ever developed the urge.

Our limitations are often magnified when we compare them to those who don’t have medical complications. And it’s hypermagnified when it’s constantly on the screen in front of us. So, I try to remind myself about a few things when the jealousy gets me down:

1. You can’t compare your behind-the-scenes to someone’s highlight reel. Just because you’re seeing friends at concerts rocking out doesn’t mean they’re not feeling a hangover the next morning. And that’s not something they’re going to share on Insta.

2. Not everything that’s posted is real. I’ll be straight with you. My skin isn’t as flawless as I make it look in pictures. Perfect 365 people! Photoshop can make anyone look stellar. Those circles under my eyes? The chapped lips? The medication bloat in my face? All magically resolved with a few clicks. Nobody is perfect, but on the Internet, we can sure make it look that way.

3. Everyone has their struggles. Your friends might be making their way across the world, but it doesn’t mean they’re not stuck in their own drama. Breakups and breakdowns are rarely played out in social media.

4. You are not on the same timeline. When jealousy arises and I see someone who has gone further in their career or has met their fitness goals, I have to stop, calm myself and remember that nobody has walked in my shoes, and nobody spends their time doing everything I need to do to make my life work. Age, experience, complications — everyone is on their own timeline for personal success.

5. Authenticity is everything. People love model Chrissy Teigen because her social media is full of truth. Body image, self-deprecating humor and openness about issues like postpartum depression are what draw people to her feed. Shame can’t survive being shared. If your struggle is real, share it!

You can always find me sharing the hot mess that is life with primary immunodeficiency at instagram.com/ilana_jacqueline!

Ilana Jacqueline is a 27-year-old dysautonomia and primary immune deficiency disease patient from South Florida. She’s been writing professionally since 2004 on everything from health and wellness to celebrities and beauty. Her blog www.letseatbetter.com is both a personal collection of anecdotes about life with chronic illness, as well as a resource for patients of all ages.
Caring for PI Children in Case of Parental Death

By Jessica Leigh Johnson

WHEN MY HUSBAND and I first became parents more than 16 years ago, we asked my sister-in-law and her husband if they’d be willing to be the guardians of our daughter, and any future children, should anything happen to us. They agreed, although at the time, they probably assumed it would be unlikely the day would come when they’d have to fulfill that promise. Since my husband and I were a mere 24 years old at the time, death seemed a long way away. Fast forward 16 years: We are now the parents of four children, three of whom have primary immunodeficiency disease (PI). Their care is expensive, time-consuming and emotionally taxing. To be honest, we haven’t revisited the subject of guardianship with my sister-and brother-in-law — mostly out of fear of rejection. Would they still want to be responsible for our kids now, knowing what a huge responsibility it would be? And if they don’t do it, who will?

Though the thought of their own death might make some parents uncomfortable, or seem like an event in the distant future, it’s crucial to have a plan in place for the care and protection of children — especially those with chronic illness and special healthcare needs.

Select an appropriate guardian. Even if parents have named a guardian for their children in the past, the diagnosis of PI or other chronic illness may change whether the chosen friends or relatives are willing to remain guardians, or whether they are the appropriate people to fill that role.

When parents die unexpectedly, children will feel most comfortable in the care of relatives such as grandparents, aunts and uncles or close friends of the family. When choosing guardians, there are specific things parents should keep in mind such as the age, health and location of the guardians. If the guardians live in another city or state, the children would have to relocate. Changing schools and making new friends after the loss of a parent might be too much stress for them. Also, consideration needs to be given to whether the guardians live near a hospital or specialty clinic where the children’s regular doctors are located. Especially during a time of custody transition, it is crucial someone familiar with the children’s condition is overseeing their medical treatment.

Parents should be completely open and upfront about their children’s illness and all that their care entails. It won’t just be the children’s lives that change in the event of parental death. The new guardians will have a huge amount of new responsibilities. Parents should ensure whoever they choose understands the children’s condition. Does the thought of caring for chronically ill children overwhelm them? Do they feel comfortable performing infusions?

Write a will. Having a will is crucial. In the will, parents legally designate the children’s guardians. If no one is listed, the courts will appoint someone. Parents can also name a trustee who can manage their assets for their children until they are of legal age.
Parents should be completely open and upfront about their children’s illness and all that their care entails.

Avoid missing medical treatments. Several manufacturers of immune globulin (IG) therapies have special programs in place to ensure there is no lapse in therapy due to a lapse in insurance coverage. Should something happen to the parents of PI children, and their insurance policy for their children is terminated, these programs exist to fill the gap by providing supplies and medication until the children are either enrolled in government-funded medical aid or added to the insurance policy of their new guardian. If parents aren’t sure whether such a program is available to them, they can simply call the manufacturer of their children’s IG therapy and ask, and then take the necessary steps to enroll. Parents should also inform the children’s potential guardians of this program, and keep a copy of the information in the document storage container along with other pertinent medical information.

Give infusion training to family members. In order for potential guardians to feel comfortable performing medical procedures on the children, they need to actually watch, and preferably even perform, an infusion or two. Being prepared in this way will eliminate mass confusion when it’s time for that first infusion. Having other family members who are able to administer infusions will also allow more freedom for parents to travel and leave their children in the care of others while they’re still living. It’s just a good idea, in general, for someone other than the children’s parents to know where the infusion supplies are kept and how to perform them if the need arises.

Planning for the event of one’s death can be an unsettling process, but making provisions for children’s financial and healthcare matters in advance will ensure their protection and bring parents peace of mind when looking toward the future.

JESSICA LEIGH JOHNSON is a stay-at-home mom and mother of four kids, three of whom have X-linked agammaglobulinemia. She is a member of American Christian Fiction Writers and has written one book about the loss of her son to a primary immunodeficiency.

References
PATIENTS WHO INFUSE immune globulin (IG) may experience side effects. One of the most common is the post-infusion headache. For some, symptoms can last for hours or even days, and while any type of headache can hinder daily activities, migraine-level pain can be especially debilitating. Often, infusion providers may ask patients to rate their level of pain to best determine a treatment plan. “The first thing we want to assess is the severity of the headache. We ask patients to rate their pain on a scale from one to 10,” says Michelle Greer, RN, IGCN, senior vice president of sales at NuFACTOR Specialty Pharmacy. “If patients have a history of migraines, they can usually tell us if they are experiencing a headache or an actual migraine.”

Pretreatment Options to Avoid Post-Infusion Pain

The patient’s regimen in the days leading up to an infusion can significantly affect how a person’s body responds during and after treatment. For example, dehydration is often at the root of many IG side effects. Experts recommend IG patients start drinking water, juice and power drinks the day before an infusion, and advise avoiding coffee and alcohol, both of which can lead to dehydration. Some patients have also seen good results from sipping electrolyte rehydration drinks, which are good to have on hand before, during and after infusions because they provide the body with necessary minerals and salts to function properly.

When it comes to premedication, taking acetaminophen (Tylenol) prior to the infusion is another way to ward off an IG headache. For patients with a history of migraines, premedication with their migraine-specific prescription can also be beneficial. For those with a medical history of severe headaches specifically triggered by IG, some physicians will also prescribe a steroid as pre- and even postmedication. In addition, lowering the rate of infusion and giving acetaminophen and antihistamines before the infusion decreases the risk of most mild side effects, including headache. In rare cases, a particularly acute form of headache resulting from aseptic meningitis can occur following IG therapy. Typically characterized by a very severe headache, fever, stiff neck and/or aversion to light (photophobia), these symptoms signal immediate medical attention should be sought.

Treating Headaches Once They Happen

For IG patients, preventing a headache is always optimal, but if a headache has already started, finding relief fast is a top priority. Here are some traditional over-the-counter recommendations:

• Nonsteroidal anti-inflammatory drugs (NSAIDS). These include medicines like aspirin, ibuprofen (Motrin, Advil) and naproxen. This type of medicine should not be taken by anyone with a history of stomach bleeding. And, a doctor or pharmacist should be consulted about possible interactions when combined with other medications.

• Acetaminophen (Tylenol). Acetaminophen may be safely taken with NSAIDs for an additive effect. Taking acetaminophen by itself is usually safe, even with a history of stomach ulcers or bleeding. It should not be taken by those who have liver disorders or three or more alcoholic drinks a day.

• Combination medications. Some over-the-counter pain relievers have been approved for use with migraine. These include Excedrin Migraine that contains acetaminophen and aspirin combined with caffeine. A similar effect can be achieved by taking two aspirin or acetaminophen tablets with a cup of black coffee.

• Migraine wraps. These flexible bands feature a removable gel pack (hot or cold) to offer therapeutic relief from headache pain.

• Aromatherapy. In this therapy, essential oils are breathed or rubbed on skin to help patients relax and change how they perceive pain. Lavender, ginger or peppermint oils are recommended to relieve headache pain.

• Magnesium. People who suffer from serious headaches such as migraines often have low levels of magnesium, and several studies suggest magnesium may prevent the wave of brain signaling, called cortical spreading depression, that produces the visual and sensory changes common when experiencing a severe headache. Taking 200 mg to 600 mg of magnesium a day can reduce the frequency of headaches. Dietary sources of magnesium include beans, whole grains, seeds, nuts and vegetables like broccoli.

Treatment Is Available

Patients who depend on IG therapy to manage chronic illness recognize side effects are something they can learn to manage. While IG-induced headaches are very common, the good news is there are also many ways to either treat them or avoid them altogether.

TRUDIE MITSCHANG is a contributing writer for IG Living magazine.
**Now Essential Oils Pure Peppermint Oil**
Peppermint oil is a therapeutic natural option for headache relief. Peppermint is known to be calming and numbing, making it helpful for people who suffer from migraine-level headaches. To use, the oil is applied to the forehead and temples. $7.99; gnc.com

**Nature’s Truth Aromatherapy Lavender Essential Oil**
New evidence shows lavender oil can effectively treat severe headaches. One recent study in *European Neurology* concluded that inhaling lavender essential oil may be an effective and safe way to relieve migraine pain. It is used by adding two to four drops of oil to two to three cups of boiling water and inhaling the vapors. A few drops can also be massaged into the skin. $6.99; bedbathandbeyond.com

**Shopping Guide to Prevent and Treat Headaches**

**Gel-Filled Migraine Wrap**
This spa-inspired migraine wrap can be securely wrapped around the head or neck. It is used by warming in the microwave or cooling in the freezer, depending on desired treatment. $4.98; walmart.com

**Nature’s Bounty Magnesium**
This neurologist-recommended over-the-counter treatment has been approved by the U.S. Food and Drug Administration for migraine relief. The formula contains a blend of acetaminophen, aspirin and therapeutically active caffeine. $9.99; target.com

**Excedrin Migraine**
This neurologist-recommended over-the-counter treatment has been approved by the U.S. Food and Drug Administration for migraine relief. The formula contains a blend of acetaminophen, aspirin and therapeutically active caffeine. $9.99; target.com
Go with Your Gut: The 5-Part Plan For Healing Gastrointestinal Issues (GERD, IBS, SIBO, Leaky Gut) & Preparing the Diseases (Inflammatory, Autoimmune) That Come With Them

Author: Mike Sheridan
Publisher: Lean Living Inc.

For many, gastrointestinal (GI) issues can progress to leaky gut and an increased risk of chronic inflammatory conditions and autoimmune diseases. But, this book discusses how GI issues can be eliminated and individuals can reduce their risk of degenerative diseases by removing foods that promote inflammation and bad bacterial growth, as well as by consuming foods that feed and support the gut and beneficial flora that live there. The book contains a five-part protocol to improve digestion, eliminate unwanted bacteria, strengthen the GI tract, re-establish healthy gut flora and provide ongoing dietary and lifestyle practices to ensure it continues.

The Autoimmune Solution: Prevent and Reverse the Full Spectrum of Inflammatory Symptoms and Diseases

Author: Amy Myers, MD
Publisher: HarperCollins Publishers

Over 90 percent of the population suffers from inflammation or an autoimmune disorder. Minor irritations like rashes and runny noses are ignored, while chronic and debilitating diseases like Crohn’s and rheumatoid arthritis are handled with a cocktail of toxic treatments that fail to address their root cause. But, in The Autoimmune Solution, Dr. Amy Myers, a renowned leader in functional medicine, offers her medically proven approach to prevent a wide range of inflammatory-related symptoms and diseases, including allergies, obesity, asthma, cardiovascular disease, fibromyalgia, lupus, irritable bowel syndrome, chronic headaches and Hashimoto’s thyroiditis.

From Crappy to Happy: The Naked Truth About Living with Celiac Disease

Author: Gluten Dude
Publisher: Amazon Digital Services

In this book, “Gluten Dude” provides guidance for those newly diagnosed with celiac disease who are “pretty much scared s***less.” He explains how eating gluten-free is not enough for bodies to heal. He discusses the pitfalls and how-tos of eating outside the comfort of one’s own home, and which spots to avoid even though they claim to be gluten-free. According to him, having the right attitude is an absolute necessity when dealing with celiac, as well as how the disease can affect relationships and how to navigate the sticky situations.

Chronic Illness Can’t Beat My Superhero Mommy

Author: Kristi Patrice Carter, JD
Publisher: Amazon Digital Services

When 7-year-old Danielle’s wonderful, loving, energetic mother was diagnosed with chronic migraines and fibromyalgia, she struggled to understand how much their lives would change. But just as they’d always done before, they adjusted. During a migraine or fibromyalgia pain flare, Danielle’s family encouraged mom to rest, assisted her with household tasks, gave gentle hugs and worked hard to support her on the days she didn’t feel well. Soon, Danielle learned just how amazing her mother really was. A chronic illness didn’t change her family’s love. It didn’t take away the mommy they’d come to know. It didn’t change her family’s hearts. Instead, it showed Danielle how strong and courageous her superhero mom was. Although fibromyalgia and migraines may steal her mom’s energy, it will never change her heart.
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- Antihemophilic Factors

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*2015 NuFACTOR is the specialty pharmacy subsidiary of FFF Enterprises, the nation’s most trusted distributor of plasma products, vaccines and other biopharmaceuticals.
Ataxia Telangiectasia (A-T)

WEBSITES
- A-T Children’s Project: www.atcp.org

Chronic Inflammatory Demyelinating Polyneuropathy (CIDP)

WEBSITES
- GBS/CIDP Foundation International: www.gbs-cidp.org
- GBS/CIDP Foundation International Discussion Forums: forum.gbs-cidp.org/forum/main-forum

Evans Syndrome

ONLINE PEER SUPPORT
- Evans Syndrome Research and Support Group: www.evanssyndrome.org

Guillain-Barré Syndrome (GBS)

WEBSITES
- GBS/CIDP Foundation International: www.gbs-cidp.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com
- GBS Support Group: www.gaincharity.org.uk
- GBS/CIDP Foundation International Discussion Forums: forum.gbs-cidp.org/forum/main-forum

Idiopathic Thrombocytopenic Purpura (ITP)

WEBSITES
- ITP Support Association – UK: www.itsupport.org.uk
- Platelet Disorder Support Association: www.pdsa.org
- KidsHealth: kidshealth.org/parent/medical/heart/kawasaki.html

Kawasaki Disease

WEBSITES
- American Heart Association: www.heart.org/HEARTORG/Conditions/More/CardiovascularConditions/Childhood/Kawasaki-Disease_UCM_308777_Article.jsp#T1T2ooPWE0
- Kawasaki Disease Foundation: www.kdfoundation.org
- KidsHealth: kidshealth.org/parent/medical/heart/kawasaki.html

Mitochondrial Disease

WEBSITES
- United Mitochondrial Disease Foundation: www.umdf.org
- MitoAction: www.mitoaction.org

Multifocal Motor Neuropathy (MMN)

WEBSITES
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

Multiple Sclerosis (MS)

WEBSITES
- All About Multiple Sclerosis: www.mult-sclerosis.org/index.html
- Multiple Sclerosis Association of America: mymsaa.org
- Multiple Sclerosis Foundation: www.msfocus.org
- National Multiple Sclerosis Society: www.nationalmssociety.org

ONLINE PEER SUPPORT
- Friends with MS: www.FriendsWithMS.com
- MSWorld’s Chat and Message Board: www.msworld.org

Myasthenia Gravis (MG)

WEBSITES
- Myasthenia Gravis Foundation of America (MGFA): www.myasthenia.org
- Genetic Alliance: www.geneticalliance.org

Myositis

WEBSITES
- The Myositis Association: www.myositis.org
- International Myositis Assessment and Clinical Studies Group: www.niehs.nih.gov/research/resources/imacs

ONLINE PEER SUPPORT
- The Cure JM Foundation: www.curejm.org
- Myositis Association Community Forum: tmacommunityforum.ning.com
- Myositis Support Group – UK: www.myositis.org.uk

Peripheral Neuropathy (PN)

WEBSITES
- Neuropathy Action Foundation: www.neuropathyaction.org
- Western Neuropathy Association: www.neuropathyhelp.org
- Neuropathy Alliance of Texas: neuropathyallianceb.org
- The Foundation for Peripheral Neuropathy: www.foundationforpn.com

Primary Immune Deficiency Disease (P1)

WEBSITES
- Immune Deficiency Foundation: www.primaryimmune.org
- Jeffrey Modell Foundation: www.info4pi.org
- The National Institute of Child Health and Human Development (NICHD): www.nichd.nih.gov/Pages/index.aspx
- American Academy of Allergy, Asthma & Immunology: www.aaaai.org
- International Patient Organisation for Primary Immunodeficiencies (IPPO) — UK: www.ipopi.org
- New England Primary Immunodeficiency Network: www.nepini.org
- Rainbow Allergy-Immunology: www.uhospitals.org/rainbow/services/allergy-immunology

ONLINE PEER SUPPORT
- IDF Common Ground: www.idfcommonground.org
- IDF Discussion Forum: idffriends.org/forum
- IDF Friends: idffriends.org
- Jeffrey Modell Foundation Facebook Page: www.facebook.com/IMFworld
- Michigan Immunodeficiency Foundation: www.immuneologist.org/en/nonprofit/243220a2ba15942e59e03d8a08709c9e-michigan-immunodeficiency-foundation-monroe

Pedicr Autoimmune Neuropsychiatric Disorder Associated with Streptococcus (PANDAS)

WEBSITES
- PANDAS/PANS Advocacy and Support: www.pas.care
- PANDAS Network: www.pandasnetwork.org
- Midwest PANS/PANDAS Support Group: www.midwestpandas.com

Pemphigus and Pemphigoid

WEBSITES
- The International Pemphigus and Pemphigoid Foundation: www.pemphigus.org

Scleroderma

WEBSITES
- Scleroderma Foundation: www.scleroderma.org
- Scleroderma Research Foundation: www.srfcure.org
- Johns Hopkins Scleroderma Center: www.hopkinsscleroderma.org

ONLINE PEER SUPPORT
- International Scleroderma Network: www.sclero.org/support/forums/a-to-z.html

Stiff Person Syndrome (SPS)

WEBSITES
- American Autoimmune Related Diseases Association Inc.: www.aarda.org
- Genetic Alliance: www.geneticalliance.org
- Living with Stiff Person Syndrome (personal account): www.livingwithspss.com
- Stiff Person Syndrome: www.stiffpersionsynrmed.net

Stiff Person Syndrome (SPS)
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